A PROSPECTIVE, OPEN LABEL, PILOT STUDY TO EVALUATE THE ROLE OF SUCRALFATE IN THE MANAGEMENT OF PRESSURE ULCERS

A DISSERTATION SUBMITTED TO THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY IN PARTIAL FULFILMENT OF THE REGULATIONS FOR THE AWARD OF M.D. DEGREE IN PHARMACOLOGY (BRANCH VI) EXAMINATION TO BE HELD IN MAY, 2018

DEPARTMENT OF PHARMACOLOGY AND CLINICAL PHARMACOLOGY

CHRISTIAN MEDICAL COLLEGE

VELLORE: 632 002, TAMIL NADU, INDIA

CERTIFICATE

This is to certify that this dissertation entitled "A prospective, open label, pilot study to evaluate the role of Sucralfate in the management of pressure ulcers" submitted by Dr. Jayanta Kumar Dey, in partial fulfillment of university regulations for the award of M.D. Pharmacology (Branch VI) degree examination of The Tamil Nadu Dr. M.G.R. Medical University, Chennai to be held in May, 2018 is a bona fide original work done under my direct guidance and supervision and completed to my utmost satisfaction.

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DECLARATION

I, Dr Jayanta Kumar Dey, do hereby declare that this dissertation entitled "A prospective, open label, pilot study to evaluate the role of Sucralfate in the management of pressure ulcers" has been done by me under the direct guidance of Dr Margaret Shanthi F.X., Professor, Department of Pharmacology and Clinical Pharmacology, Christian Medical College, Vellore and Dr. Henry Prakash, Professor, Department of Physical Medicine and Rehabilitation, Christian Medical College, Vellore in partial fulfillment of university regulations for the award of M.D. degree in Pharmacology (Branch VI). I have not submitted this dissertation in any part or full to any other university or towards any other degree.

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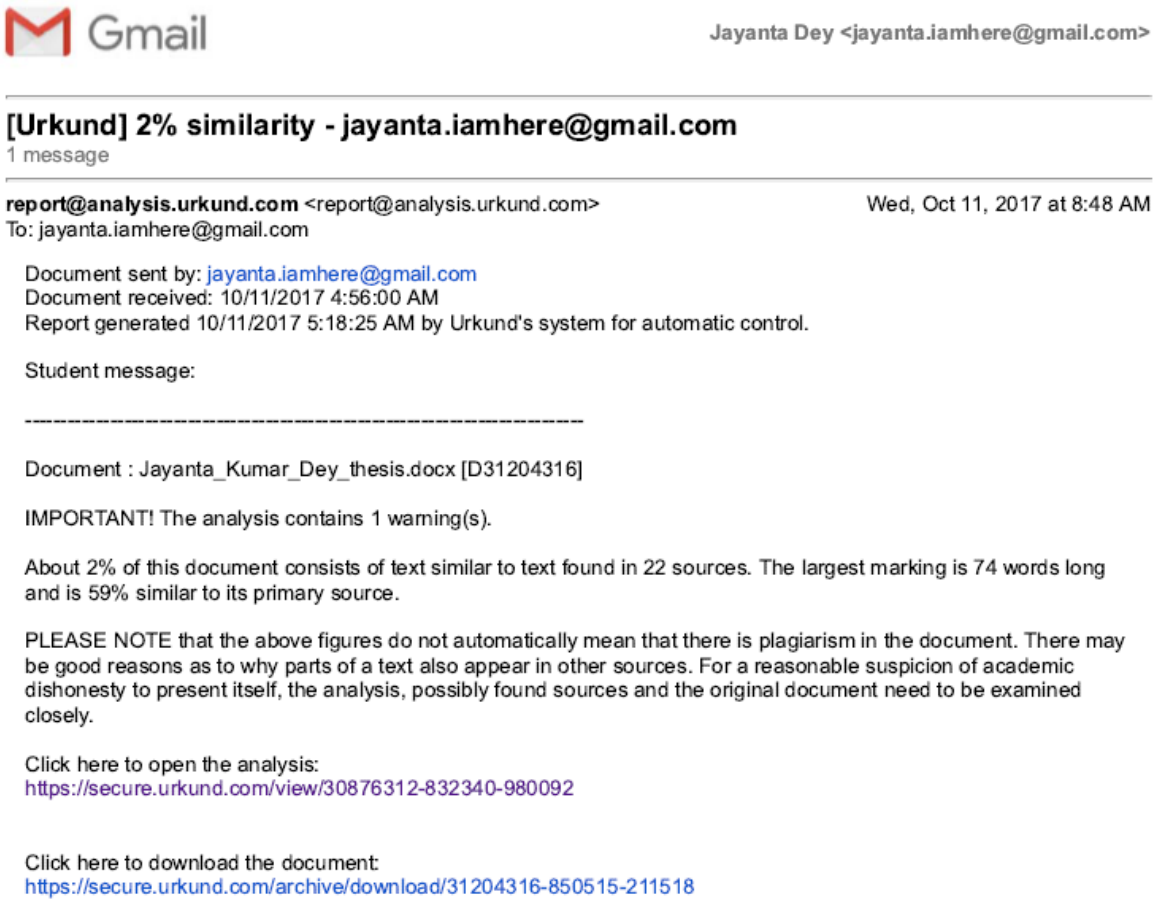

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FREQUENTLY USED ABBREVIATIONS

Abbreviation	Expansion
RGBD	Red Green Blue Depth
EGFr	Epidermal Growth Factor receptor
ICMR	Indian Council of Medical Research
NPUAP	National Pressure Ulcer Advisory Panel
PLY	Polygon File Format
PUSH	Pressure Ulcer Score for Healing

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Abstract

Introduction: Pressure ulcers are a common problem in patients with neurological disorders and prolonged immobilization, which leads to significant morbidity, occasional mortality with long hospital stay and expenses.

Present Scenario: Currently, the standard treatment provided is normal saline dressing for clean non-infected pressure ulcers. Topical Sucralfate has been used to heal burn wounds and various dermatological conditions like erosive dermatitis, aphthous stomatitis, intertrigo and acute radiation esophagitis. The results of these clinical trials have been positive in favour of Sucralfate.

Objectives: In this study, we determined if Sucralfate increases the rate of healing of pressure ulcers (grade 3) in comparison to normal saline.

Patients and methods: Patients matching inclusion criteria were divided into two groups. The control group received conventional normal saline dressings (present standard of care) and the intervention group received 7% Sucralfate ointment. The Sucralfate ointment was prepared by the institutional pharmacy. An assessor scored the wound (PUSH Tool 3.0), take tracings of ulcer perimeter on a transparent sheet for area calculation and volume of ulcers on day 1, day 7 and after the completion of the study (Day 14). The volume on analysis days was assessed using a custom program developed by the Department of Bioengineering, CMC, Vellore using Microsoft Kinect.

Results and conclusion: Both descriptive and analytical statistics were carried out. The percentage change in area and PUSH 3.0 score were found to be significant in the Sucralfate group. However, due to a lesser sample size, the baseline area and volume had variation. As a result, the percentage decrease in volume in the Sucralfate group was not significant; although the median of percentage decrease in Sucralfate group was much more when compared with the percentage decrease in the normal saline group.

Introduction

A pressure ulcer or injury is a lesion which occurs due to pressure resulting in damage of underlying tissue. These are regions of localized damage to the skin and underlying tissues that can occur over bony prominences such as the heels or sacrum. These are an important source of suffering for not only patients but also their caregivers.(1–3) These sores have existed since the dawn of our infirm species. J Thompson Rowling has described pressure sores in unearthed Egyptian mummies in 1961(4), and even in the early 1800s scientific writings have addressed them. They continue to be an ever-present problem within our society. The prevalence of pressure sores in hospitalized has been reported to be from 3.5% to 69% in each type of clinical setting.(5–8)

Pharmacoeconomically the cost to heal a single full-thickness pressure injury might go as high as 70,000 dollars.(9) Considering Indian scenario the cost of managing such ulcer per hospital admission of 12 weeks is approximately 1,75000 INR.(10) The significance of pressure ulcers is that apart from imposing a restriction of movements and hence creating a vicious cycle in the healing process, these ulcers are of significant importance in decreasing the quality of life and increase the costs of treatment in these patients.(11) The terms bedsore, pressure sore and decubitus ulcer are often used interchangeably in the medical community. The term Decubitus comes from the Latin word “decumbere”, means “to lie down”. Decubitus ulcers, hence

occur at sites overlying bony structures which are prominent when the person is lying in recumbent position. It might occur on the hip, tailbone, back, scalp or any other area to which pressure is applied while a person is lying down. Therefore, decubitus ulcer does not adequately describe ulceration that occurs while in other positions as prolonged sitting.(12) Pressure from prolonged sitting may cause an ulcer over the ischial tuberosity. Because the common denominator of all such ulcerations is pressure, thus the term that best describes this condition is pressure sore. In recent times, the term pressure ulcer has been revised to pressure injury.(13)

Coming to the prevalence of pressure sores, it appears to be bimodal in distribution. A small peak occurs during the third decade of life reflecting traumatic neurologic injury. As the patients move to the age category of 75 years or more, a larger incidence of pressure ulcer occurs.(14) Two-thirds of pressure sores occur in patients older than 70 years.(15)

Tissues are capable of withstanding enormous pressures, but only briefly. Prolonged exposure to pressures just slightly above capillary filling pressure initiates a series of events which ultimately leads to tissue necrosis and ulceration.(16) The inciting event is compression of the tissues against an external object such as a mattress, wheelchair pad, bed rail, or another surface.

Pressure ulcers are now considered a good indicator of quality of care and in many places, the failure to prevent or heal them can lead to litigation.(17)

Primary factor being external pressure, in particular, non-uniform pressure, such as those occurring over bony prominences which have less soft tissue coverage will cause tissue distortion which that can cause tissue distortion tending to collapse regional vasculature. The pressure required to occlude blood flow over hard sites is roughly half than that required in soft tissue.(18)

The current treatment of pressure ulcers is associated with pain, and prolonged period of time for natural healing process, which is only effective if pressure is lifted from the site of ulcer.(19)

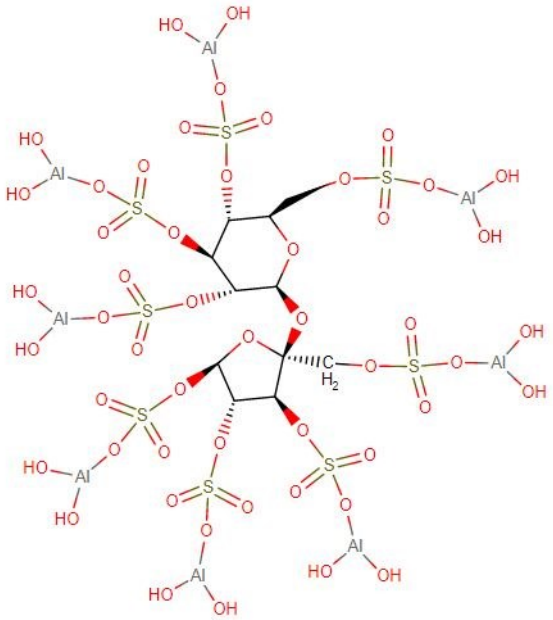
Relapse can only be prevented if sufficient perfusion and blood supply of underlying tissues is maintained otherwise any treatment would be temporary and the ulcers are to re-appear with restoration of pressure.(20)

Conventional treatments include measures such as irrigation with normal saline and sterile dressing while more expensive methods include platelet growth factors, recombinant DNA, hydrogel, or physical modalities like ultrasound, ultraviolet light and even LASER. Stage III and above usually require surgical procedures such as skin graft. The consensus of opinion is that pressure ulcers must be avoided by preventive measures in the first place.(21)

Dressings are a major component in the management of a pressure ulcer. Maintenance of a moist wound environment is the primary goal of a dressing.(22) Although non-gauze dressings are more expensive than gauze dressings, less frequent dressing changes faster healing rates, and lower incidence of infections make non-gauze-based dressings more cost-effective over time.

The study drug Aluminium sucrose octasulfate or Sucralfate has been approved by FDA for the treatment of active duodenal ulcers in oral tablet and suspension form. Off-label uses include its use in oesophagitis and adjunct therapy in peptic ulcer.

The chemical structure of this drug is shown below (*Adapted from Drugbank*).(23) **Figure: 1** Molecular structure of Sucralfate



Its IUPAC name is Hexadeca-μ-hydroxytetracosahydroxy[μ8-[1,3,4,6-tetra-O-sulfo-β-D-fructofuranosyl-α-D-glucopyranoside tetrakis(hydrogen sulfato)(8-)]]hexadecaaluminum. Its mechanism in healing ulcers in gastrointestinal tract include forming a complex by attaching to positively charged proteins in exudates leading to the formation of a viscous paste-like adhesive substance. This sticky substance locally forms a protective coating to protect the gastric mucosa against peptic acid, pepsin and bile salts.

Since, Sucralfate causes healing of peptic ulcers, over the next couple of decades it was investigated for the treatment of various other types of lesions. Those include radiation oesophagitis, diaper rash in children, oral, vaginal, rectal lesions, Behcet's disease and most recently in burn wounds. The molecular mechanism of Sucralfate indicated that it had the potential to heal chronic wounds. Also, the price of Sucralfate is cheap when compared to various kinds of dressings which are used for the treatment of pressure ulcers. The fixed drug combination of Sucralfate with metronidazole is available for topical use in our country for the treatment of various ulcers. In a view to its cheap price and the need of newer therapies in the treatment of pressure ulcers, we proposed this study to use Sucralfate as a topical agent in the treatment of pressure ulcer in comparison to the standard of care(normal saline) provided in our hospital.

Hypotheses

When topical Sucralfate is used as a 7% Ointment for the treatment of pressure ulcers, due to its molecular mechanism of action viz. increasing epidermal growth factor and basic fibroblast growth factor, inducing dermal fibroblasts and keratinocytes, inhibiting release of interleukin-2 & interferon- γ from damaged skin cells and stimulating factors required for angiogenesis; it will heal the pressure ulcer faster with less requirement of prolonged hospitalization and expensive surgery.

The faster healing rate can be quantified as a decrease in ulcer area, PUSH 3.0 score and volume when compared with the normal standard of care used.

Aim and objectives

The aim of this study was to prove that application of topical 7% Sucralfate ointment helps in better healing of bed sores located over various bony protuberances in bed-ridden patients.

Primary Objective/Outcome was:

To compare the healing effect of topical Sucralfate with normal saline (standard of care) in pressure ulcers.

i. To compare the change in the area of pressure ulcers when treated with Sucralfate or Normal Saline.

ii. To compare the change in PUSH 3.0 score of pressure ulcers when treated with Sucralfate or Normal Saline.

iii. To compare the change in volume of pressure ulcers when treated with Sucralfate or Normal Saline.

Secondary Objective/Outcome was:

To measure the blood Aluminium levels in four random patients from each group.

Review of literature

Historical Background

Pressure sores are also known as pressure ulcers, decubitus ulcers. These were earliest documented by Hippocrates in 400BC, later they were described as 'gangraene' in bedridden patients by Fabricius Hildanus in 1593. Around 1777 Wohlleben referred to this pathological condition as 'gangraena per decubitum': tissue necrosis by lying down. However, they must have been known long before, given their description in Egyptian mummies by Thomas Rowing.(24)

Definition

An ulcer is a break in the continuity of the covering epithelium-skin or the mucous membrane. It may either follow the molecular death of the surface epithelium or its traumatic removal.(25)

Pressure sores are now defined as localized areas of tissue degeneration in the skin or the underlying tissue, resulting from a prolonged mechanical load, but their development may involve many possible contributing factors, like tissue conditions, temperature and humidity, that influence pathological processes.(26)

A pressure ulcer is a local injury to the skin and underlying tissue, that happens over a bone, due to unrelieved pressure. It ranges from erythema of the skin to severe, deep ulcers with exposure of underlying tissue i.e. muscle or bone. Pressure ulcers significantly threaten the well-being of patients with limited mobility.(22)

Morbidity and Mortality

Pressure ulcers have affected mankind for ages, addressing the overall management of pressure ulcers is now a leading national healthcare issue. Although we have developed many advances in medicine, surgery, nursing care and self-education about its management, pressure ulcers remain a major cause of morbidity and mortality. This is more evident in persons with impaired sensation, prolonged immobility, or advanced age.

Patients predisposed to pressure ulcers are at high risk of morbidity and mortality. The relative mortality of those with pressure sores has been reported to be five times higher than those without sores. Studies have shown pressure sores to be a primary cause of death in as many as 6% of patients admitted to geriatric wards and a major contributing factor in a further 6%.(27)

Epidemiology, Incidence and Prevalence

Within acute care in the west, the incidence of bedsores is 0.4% to 38%; within long-term care, 2.2% to 23.9%; and in home care, 0% to 17%. There is the same wide variation in prevalence: 10% to 18% in acute care, 2.3% to 28% in long-term care and 0% to 29% in home care. There is a much higher rate of bedsores in intensive care units because of immunocompromised individuals, with 8% to 40% of ICU patients developing bedsores.(5)

The incidence in hospitalized patients ranges from 2.7% to 29%, and the prevalence in hospitalized patients is 3.5% to 69%. Patients in critical care units have an increased risk of pressure ulcers, as evidenced by a 33% incidence and 41% prevalence.(6,28–31) Patients with pre-existing pressure ulcers demonstrate a 26% incidence of additional pressure ulcer formation over a 6-month period. The incidence in chronic care hospitals is reported to be 10.8%.(32)

As per Fuhrer et al. persons with spinal cord injury (SCI) associated comorbidity are also at increased risk. The incidence of pressure ulcers in this population is in the range of 25-66 %.(33) Those having higher level SCI lesions carry a greater risk of developing pressure ulcers than those with lower-level lesions. Of 100 patients with pressure ulcers, 33 had ulcers that were classified as stage 2.(34)

Etiology

Numerous diverse factors interact to cause pressure ulcers. These factors can be classified a pathomechanical or pathophysiologic.

Pathomechanical Factors (Extrinsic or Primary)

Prolonged Pressure

As obvious, the most contributing factor in developing pressure ulcers is pressure itself. The ulcers arise from prolonged tissue ischemia caused by

pressure that exceeds the tissue capillary pressure. Over long periods of time pressure deprives tissues of oxygen and vital nutrients, leading to ischemia and hypoxia, which then causes the necrosis and ulceration.(35)

Interface Pressure

Interface pressure remains an ambiguous factor in the development of pressure ulcers. Defined as “perpendicular force per unit area between the body and support surface” by NPUAP, interface pressures less than 32 mm Hg are assumed by many clinicians to be safe, pressures in excess of 32 mm Hg are thought to lead to closure of capillary beds which in turn leads to ischemia and reperfusion injury notably in the muscle, which develops the lesion and eventually ulcerates. This ischemia-reperfusion mechanism ultimately leads to neutrophil-mediated inflammatory tissue destruction, most likely a free radical injury that eventually causes pressure ulceration.(26,36,37)

Shear

It is a mechanical stress directed parallel to the plane of interest. Shearing forces have been implicated as pathomechanical contributors in the development of pressure ulcers, especially those on the sacrum. Though scientific evidence is lacking, it is logical to conclude that the angular and vertical force that occurs downward when patients are in a semi-upright position in bed tends to distort

the tissues and blood vessels near the sacrum, placing this region at risk for tissue breakdown.(38,39)

Friction

It is the force of two surfaces moving across one another. Friction and the increased drag coefficient that occurs when moving patients across bed sheets and other support surfaces can cause microscopic or macroscopic tissue trauma. Moisture, maceration, and tissue breakdown increase the surface tension of the skin and the support surface leading to the more susceptible to pressure, shear, and friction damage.(40)

Immobility

Immobility is a major extrinsic factor associated with the risk and formation of pressure ulcers. Immobility in bedridden patients tends to cause pressure ulcers on the sacrum, occiput, heels, malleoli, and trochanteric regions, whereas patients using wheelchairs for mobility, tend to develop pressure ulcers over ischial tuberosity.(41)

Pathophysiological Factors (Intrinsic or Secondary)

Pathophysiological factors underlying pressure ulcers include fever, anaemia, infection, ischemia, hypoxemia, hypotension, malnutrition, SCI, neurologic disease, decreased lean body mass, and increased metabolic demands. Nutrition

and anaemia are important factors in the healing and prevention of pressure ulcers.

Pathophysiology

The pathogenesis of pressure sores lacks clarity. Tissue changes have been divided into primary changes, which are either mechanical or physiological in nature, and secondary changes, which may follow primary changes, usually within 24 hours. Secondary changes are defined as being reversible (e.g. oedema) and damage being irreversible (e.g. tissue necrosis).(24)

Primary mechanical changes

Primary mechanical changes involve the pressures, stresses, strains, and fluid and ion flows within the tissue as a consequence of the externally applied mechanical load. Fluid and ion flow will result in altered ion concentrations and concentrations of nutrients dissolved in the interstitial fluid. The primary changes determine the internal load of the tissue for the tissue damage. The degree of primary changes due to external loading is dependent on the type intensity of loading as well as on the amount of ground substance and fibre content and organization in the interstitial space of the tissue.(35)

Primary physiological changes

As a consequence of altered internal load, several primary physiological changes occur in the tissues like increased tissue pressure. Initially, a rise in tissue pressure causes a corresponding rise in local blood and lymph vessels. Consequently, fluid leaks out from the microcirculation and lymphatic drainage is enhanced. With increasing pressure the blood will close or even collapse, resulting in tissue ischemia and accumulation of waste products within minutes. Together with the diminished supply of nutrients due to interstitial fluid flow, this may lead to a serious disturbance of the metabolic equilibrium of the tissue. Muscular tissue due to its high metabolic rate is particularly susceptible to this metabolic stress. However external loads for occlusion of both blood and lymph vessels are relatively low i.e. 8-12 kPa.(35)

Secondary physiological changes

With maintained load or several hours after prolonged mechanical loading, a range of secondary changes and indicators of damage are found. Oedema is formed rapidly in all tissue layers. Oedema enlarges the distance between capillaries and muscle cells, thereby impeding the transport of oxygen and nutrients to the cell. Besides the formation of oedema, a decrease of cross-striations and myofibrils, hyalinization of fibres and infiltration by neutrophils and macrophages are observed.(24) Hyalinization is accompanied by damage to

the mitochondria, the sarcoplasmic reticulum, and the plasmalemma within the muscle fibres. The presence of neutrophil and macrophages points at the defence mechanism of the tissue.(35)

Kosiak et al. in an experiment subjected to dogs concluded that intense pressure of short duration was as injurious to tissues as the lower pressure applied for longer periods of time. He also concluded that prolonged pressure was the direct and primary cause of pressure ulcers.(35)

Dinsdale et al. analyzed the role of pressure and fiction in the production of pressure ulcers in healthy and paralyzed pigs and concluded that friction is a factor in the pathogenesis of decubitus ulcers since it applies mechanical force in the dermis. Minimal changes occurred with intermittent pressure relief, even at pressures of 240mm Hg.(36)

Staging of Pressure Ulcer

The staging system produced by the National Pressure Ulcer Advisory Panel

Stage I: An observable pressure-related alteration of intact skin whose indicators when compared with the adjacent area may include one or more changes in tissue consistency, skin temperature and/or sensations. The ulcer appears as defined redness in the lightly pigmented skin, whereas in darker skin tones it might appear purple or blue hues.

Stage II: Partial thickness skin loss involving epidermis or dermis, or both. The ulcer is superficial and presents clinically as an abrasion, blister, or shallow crater.

Stage III: Full-thickness skin loss involving damage or necrosis of subcutaneous tissue, that may extend down but not through underlying fascia.

Ulcer might or might not have undermining into adjacent tissue.

Stage IV: Full thickness skin loss with extensive destruction, tissue necrosis, or damage to muscle, bone, or supporting structures like tendon, joint capsule.(42)

Treatment of Pressure Ulcers

The cornerstone in healing a pressure ulcer is turning and repositioning the patient through pressure relief. Patients who are capable of shifting their weight every 10 minutes should be encouraged to do so. Repositioning should be done every 2 hours, even in the even if using any special beds or surface. Efforts should be made to avoid sliding the patient over a surface to prevent shear forces and friction. Patients who develop a pressure sore while sitting should be placed on bed rest with frequent repositioning.(43)

Pressure reduction can be done through the use of specialized support surfaces for bedding and wheelchairs which will maintain tissue pressures less than 30mm Hg. These specialized surfaces include foam devices, air-filled devices,

water-filled devices, gel-filled devices, low air-loss beds and air-fluidized beds.(37,39)

Wound Dressings

Wound dressings vary with the state of the wound and the idea is to achieve a clean, healthy wound with granulation tissue.

- Hydrocolloid dressings form an occlusive barrier over the ulcer while maintaining a moist wound environment and prevention bacterial contamination. A gel is formed when wound exudate comes in contact with the dressing. It also prevents friction and shear.
- Transparent adhesive dressings provide a moist wound setting and prevent bacterial entry along with promoting epithelization.
- Alginate dressings are fibrous products derived from brown seaweed and are available in nonwoven sheets and ropes. Alginate forms a gel when it comes in contact with wound drainage, and may be used in both non-infected of infected wounds.(38)
- Gel dressings are available in sheet form, in granules, and as a liquid gel. They keep the wound surface moist as long as they are not dehydrated.

Debridement

Removal of necrotic tissue is an absolute must in the treatment of pressure sores. Since dead tissue is ideal for bacterial growth, it has the ability to inhibit wound healing. There are multiple ways to excise necrotic tissue.(44)

- Autolytic debridement is the use of moist dressings to promote autolysis with body's own enzymes. It is a slow process, but painless.
- Biological debridement or maggot debridement therapy is the use of medical maggots to feed on necrotic tissue and therefore clean the wound of excess bacteria. Although this fell out of favour for many years, in January 2004, maggots were approved as a live medical device.(45)
- Chemical debridement, or enzymatic debridement, uses various chemical agents that act by attacking collagen and liquifying necrotic wound debris without damaging granulation tissue.(46) Proteolytic enzymes are used to chemically debride wounds. The action of these enzymes is aimed specifically at the necrotic tissue.
- Mechanical debridement is a method in which necrotic tissue is removed after loosening and is accomplished by whirlpool treatments, forceful irrigation,(47) or use of wet to dry dressings.
- Sharp debridement is the removal of necrotic tissue with a scalpel or similar instruments.

- Surgical debridement is the most popular method, as it allows the surgeon to quickly remove the dead tissue with little pain to the patient. It, however, requires a great deal of clinical skill.

Surgical Approach

Several options are available for management of pressure ulcers, including direct closure, skin grafting, skin flaps and musculocutaneous flaps. In surgical method, both skin and soft tissue coverage can be given. Flaps which contain muscle provide a physiological barrier to infection. Improved vascularity enhances local oxygen tension, provides extended soft tissue penetration for antibiotics and improves total lymphocyte function.(48,49)

Direct Closure

Although direct closure is the simplest procedure, since the ulcers are usually wide, hence these cannot be closed by a direct primary closure. Since these wounds are tense as a result of large tissue defects, the direct closure can lead to excessive wound tension and the paucity of soft tissue coverage. Tissue expanders have been used to provide adequate skin surface and to facilitate the closure of the wound(50–52) such as:

- Skin grafts
- Skin Flaps
- Musculocutaneous flaps

- Free Flaps

Physiotherapy

A wide variety of physiotherapy treatment approaches have been incorporated in pressure sore management. Modalities like ultraviolet radiation, ultrasound, superficial conductive heat, hyperbaric oxygen therapy, whirlpool bath, electrical stimulation, even LASER(in experimental studies) have been used.

Wound Healing

The healing procedure involves either healing by primary intention or by secondary intention.(53) Clean, surgically controlled wounds can be healed by primary intention. Healing of this type of wound only requires re-epithelization. Wounds that have complicating factors which prevent healing by secondary intention such as contamination, infection fill the crater or gap by the formation of granulation tissue.(54) Usually, pressure ulcers, abscesses or large surface wounds fall in this category. The closure, in this case, occurs via contracture.

The healing method is a highly dynamic process and involves complex interactions of extracellular matrix molecules, soluble mediators, various resident cells, and infiltrating leukocyte subtypes. The immediate goal in repair is to achieve tissue integrity and homeostasis.(55) To achieve this goal, the healing process involves three phases that overlap in time and space: inflammation, tissue formation, and tissue remodelling. In the process of

inflammation, platelet aggregation occurs first followed by infiltration of leukocytes into the wound site. In tissue formation, epithelialization and newly formed granulation tissue, consisting of endothelial cells, macrophages and fibroblasts, begin to cover and fill the wound area to restore tissue integrity. Synthesis, remodelling, and deposition of structural extracellular matrix molecules are indispensable for initiating repair and progression into the healing state. Wound repair depends on neoangiogenesis, the activation of local immune response, and in the presence of growth factors including epidermal growth factor (EGF), transforming growth factor β(TGF-β), and basic fibroblast growth factor(bFGF).(56–60)

Sucralfate is known to have multiple beneficial effects on wound healing. This drug induces the proliferation of dermal fibroblasts and keratinocytes in vitro and inhibits the release of interleukin-2 and interferon-γ from damaged skin cells.(61) The physical barrier feature of Sucralfate is to diminish inflammatory reaction and improve mucosal healing.(62–65) Limiting the inflammation might decrease fibrosis and stricture formation and EGF expression as well as the expression of other factors involved in tissue repair processes.(66) Stimulating effects on vascular factors, such as angiogenesis, which play important roles in tissue repair, have been demonstrated by Sucralfate.(67,68)

Studies showing the role of Sucralfate in the healing of wounds include:

- Sucralfate does not have any adverse effects(69) thus it is widely employed in clinical practice to prevent or treat recurrent aphthous stomatitis and several gastrointestinal diseases.(70,71)
- Usefulness of topical Sucralfate on peristomal and perineal excoriations was demonstrated.(72) Markhan *et al.* reported the effect of topical Sucralfate 4% aqueous cream treatment on erosive dermatitis, which developed in the perineal area.(73)
- Recently, the potential role of Sucralfate as a topical agent to treat intertrigo, a superficial inflammatory dermatitis involving juxtaposed skin surfaces to friction, heat, moisture and maceration was evaluated.(74)
- Three patients with vaginal ulceration were treated with vaginal douches of Sucralfate 10% suspension twice daily.(75)
- Sucralfate topical treatment decreased significantly the frequency, healing time, and pain of oral ulceration and the healing time and pain of genital ulceration.(76)
- Lin *et al*. by reviewing the topical or intralesional treatment for mucocutaneous lesions in Behçet's disease, include Sucralfate among

the different drugs, which are considered safe and useful for the treatment of mild to moderate mucocutaneous disease.(77)

- There was significant reduction in pain after application of topical sucralfate post hemorrhoidectomy and earlier wound healing compared with that of placebo.(78)
- Etiz *et al.* as well demonstrated that head and neck cancer patients undergoing radiotherapy and receiving Sucralfate (six daily doses of the oral suspension of 1 g) had a reduction in oral mucositis.(79)
- Sur *et al.* reported that Sucralfate (10% Sucralfate suspension) was used in the management of acute radiation esophagitis.(80)
- The role of the topical use of Sucralfate in the treatment of burn wounds was investigated by Banati *et al.*(81)

Toxicity of Sucralfate: The study by Banati *et al.*(81) reports burned patients who used a 7% Sucralfate cream for burn wound dressing twice daily did not show detectable serum Aluminium levels in their blood samples. Sucralfate is an effective agent for burn healing and it has no toxicity. Almost all studies have indicated the safe and effective behaviour of this compound.(69) Sucralfate has also been shown to have antibacterial activity.(82)

Mechanism of Sucralfate in Wound healing:

The drug adheres to the epithetical proteins at the ulcer site. This then forms a protective coating against the environment. Sucralfate increases both epidermal growth factor and basic fibroblast growth factor concentrate in the wound.(61) Sucralfate can bind basic fibroblast growth factor, thus protecting its degradation and allowing it to act as an angiogenetic molecule.(83) Sucralfate is able to stimulate the synthesis and release of epidermal growth factor which in turn stimulates healing and affects prostaglandin synthesis.(66) It has also been indicated that Sucralfate induces the proliferation of dermal fibroblasts and keratinocytes *in vitro*, and inhibits the release of interleukin-2 and interferon-γ from damaged skin cells.(61)

Prostaglandin E2 synthesis is enhanced in keratinocytes and dermal fibroblasts by Sucralfate which is responsible for the augmentation of the healing process.(61) Synthesis of collagen in fibroblasts is controlled by Sucralfate.(84) Stimulating effects on vascular factors, such as angiogenesis, which play important roles in tissue repair, have been demonstrated by Sucralfate. (68)Sucralfate can be used as an adjunctive or alternative agent in pressure ulcer healing therapies in the future.

Hence, the present study was taken up to investigate the efficacy of topical application of Sucralfate for the healing of PUs in comparison to normal saline.

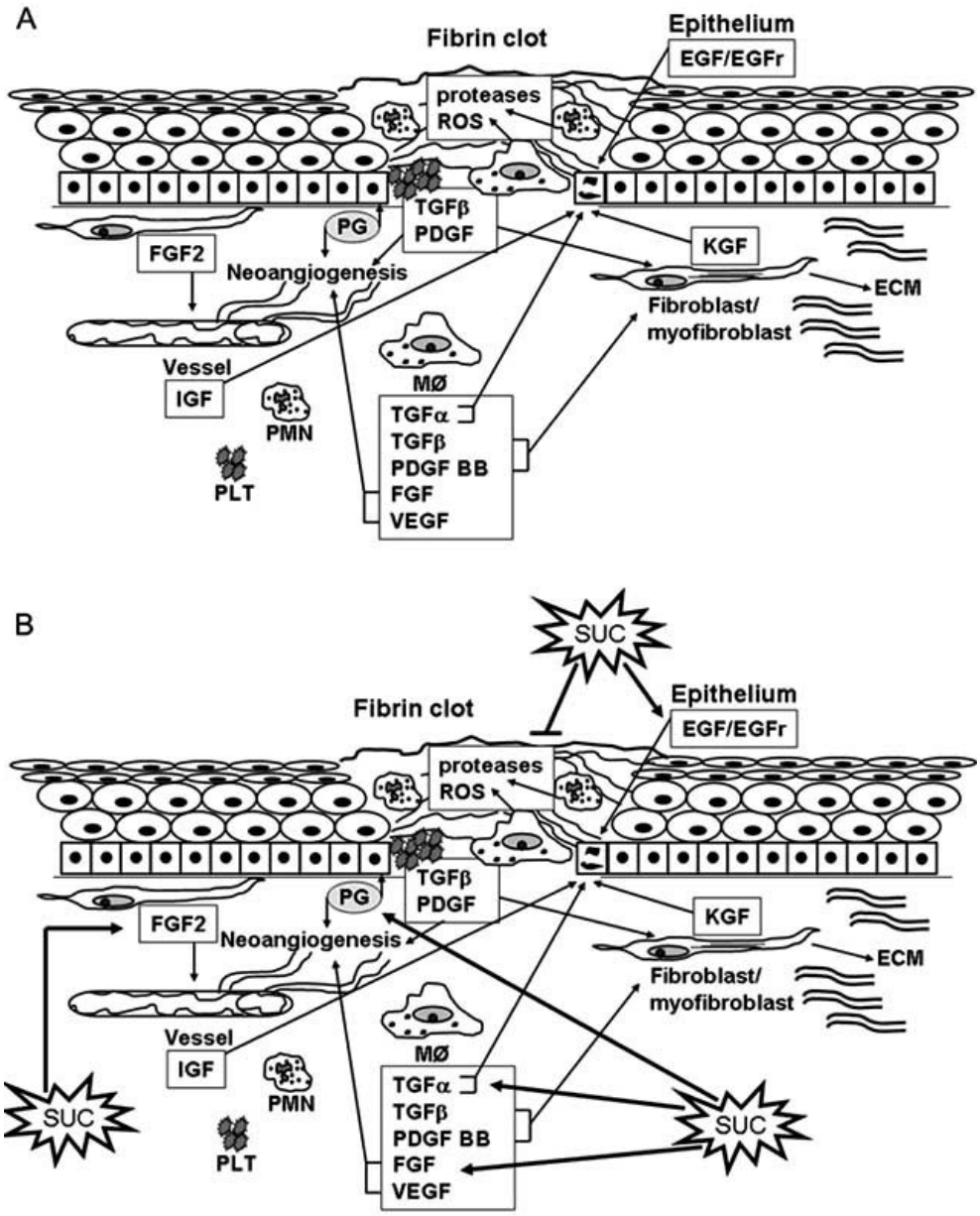


Figure: 2 [Molecular mechanisms of action of Sucralfate in epithelial wound healing.](85)

(*Adapted from* Masuelli et al.)

A. The release of growth factors involved in the epithelial wound healing process.

B. Sucralfate increases growth factors bioavailability and prostaglandins and decreases the production of oxygen free radicals synthesis, thus potentiating angiogenesis, granulation tissue, and re-epithelialization. EGF: Epidermal Growth Factor; EGFr:Epidermal Growth Factor receptor; ROS: Reactive Oxygen Radicals; ECM: Extracellular Matrix; PDGF: Platelet-derived Growth Factor; TGF-: Transforming Growth Factor-; KGF: Keratinocyte Growth Factor; FGF2: Fibroblast Growth Factor 2; TGFα: Transforming Growth Factorα, PDGF BB: Platelet-derived Growth Factor BB; FGF: Fibroblast Growth Factor; VEGF: Vascular Endothelial Growth Factor; IGF: Insulin-like Growth Factor; PG: Prostaglandins; PLT: Platelets; PMN: Neutrophil granulocytes; MØ: Macrophages; SUC: Sucralfate

Patients and methods

The work was started after getting the approval of the Institutional Review Board, Christian Medical College, Vellore, Universal Trial Number (U1111-1177-8421) from International Clinical Trials Registry Platform, World Health Organization and registration number [CTRI/2016/03/006745; Registered on 21/03/2016] from Clinical Trial Registry-India, National Institute of Medical Statistics, ICMR.

It was performed according to the Good Clinical Practice guidelines and the Declaration of Helsinki.

Here, the intervention agent used was Sucralfate ointment (7%) on the pressure ulcer as a dressing. The comparator group received Normal Saline dressings. We were not using a new molecular entity or new chemical entity on vulnerable subjects. Hence, as per newest guidelines of consent taking by CDSCO dated 31st July 2015 we took written consent.

Once we obtained informed consent and eligibility criteria were fulfilled the treatment group received Sucralfate ointment (7%) dressing with sterile gauze and pad once every day for a total duration of 14 days. The comparator group received Normal Saline dressings with sterile gauze and pad for the same duration.

The ulcer healing rate was assessed using the **P**ressure **U**lcer **S**core for **H**ealing (PUSH 3.0 score). PUSH 3.0 scores pressure ulcer from 0 to 17 based on ulcer surface area (length × width), exudate amount and tissue type.(86,87)

The first sub-score ulcer surface area was calculated by multiplying the maximum length and maximum breadth which were measured using a ruler.

The second sub-score, i.e. exudate amount was estimated on the removal of the dressing prior to application of the intervention or comparator agent.

The third and final sub-score was calculated based on the type of tissue, i.e. necrotic, slough, granulation, epithelial and closed.

After all the three sub-scores were calculated, we scored the final PUSH 3.0 score for each patient every time a reading was taken.

It is shown in figure 3

LENGTH X WIDTH (in cm^2)	**0** 0	**1** < 0.3	**2** 0.3 – 0.6	**3** 0.7 – 1.0	**4** 1.1 – 2.0	**5** 2.1 – 3.0	**Sub-score**
		6 3.1 – 4.0	**7** 4.1 – 8.0	**8** 8.1 – 12.0	**9** 12.1 – 24.0	**10** > 24.0	
EXUDATE AMOUNT	**0** None	**1** Light	**2** Moderate	**3** Heavy			**Sub-score**
TISSUE TYPE	**0** Closed	**1** Epithelial Tissue	**2** Granulation Tissue	**3** Slough	**4** Necrotic Tissue		**Sub-score**
							TOTAL SCORE

Figure: 3 The PUSH 3.0 scoring system to record the healing of a pressure ulcer

The PUSH 3.0 scores were calculated on days 0, 7 and 14 for either group.

To measure ulcer size, tracings of ulcer perimeters were taken on surgical spirit cleaned transparent sheets on days 0, 7 and 14 using a permanent marker. A reference 1cm line was drawn using a ruler to each transparent sheet. Once, the ulcer perimeter readings were taken each transparent sheet was scanned using HP LaserJet Pro M1136 Multifunction Printer and scanner. Each scan was saved in jpeg format with 300 dpi resolution. The scanned tracings of ulcer perimeters were further analyzed using Digimizer 4.6.1, an open source software by Medcalc Software bvba, Belgium.

Once, the reference line was measured initially, then multiple points were added to the perimeter of the ulcer tracing manually, which led to the calculation of the area of each wound. A screenshot of the software in use is shown in figure 4.

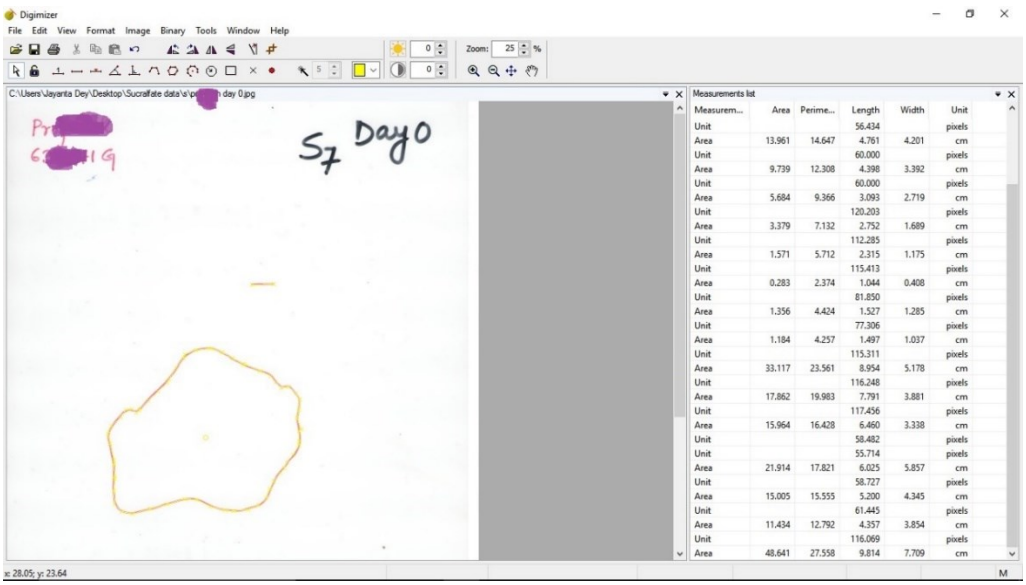


Figure: 4 A screenshot from the open source software Digimizer used to analyze ulcer area

This was also done for both the groups.

To measure ulcer volume, we used the Microsoft Kinect 2.0 RGBD scanner.

Kinect-based Wound Scanning and Quantification

In order to quantify the volume of a pressure ulcer, one needs a detailed scan of the topology of the wound surface. In this work, we used the Microsoft Kinect 2.0 RGBD scanner to scan pressure wounds. The Kinect uses a high-resolution 1080p RBG camera along with a depth sensor that uses time-of-flight technology for measuring the depth of objects in the environment.

It is shown in figure 5

Figure: 5 The Microsoft Kinect device along with its power adapter and USB 3.0 connector

A custom program was developed by the Department of Bioengineering at CMC, Vellore to scan wound surface data using the Microsoft Kinect 2.0. A screenshot of the custom program is shown in Figure 6, which was developed by modifying an existing program available from the Kinect SDK from Microsoft. The program has the capability to scan and save surface scans for different patients on different days (day 0, day 7 and day 14). The program can be configured to scan and store data at different resolutions, with co-registered RBG and depth images. The data from the program is saved in three data formats – STL, OBJ and PLY – which are standard file formats for storing 3D data.

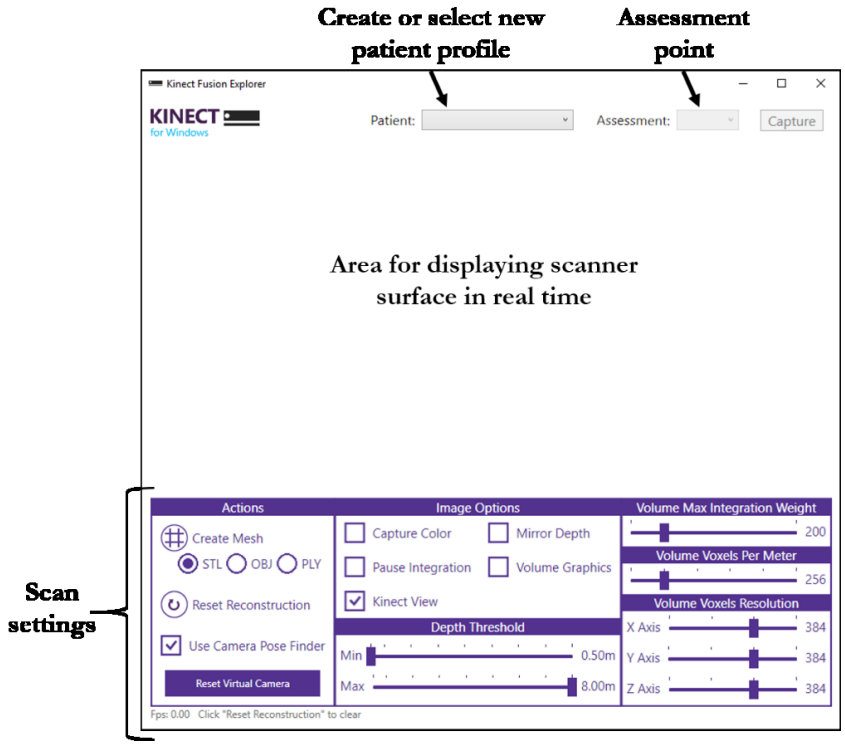


Figure: 6 Screenshot from the custom program that was used to analyze ulcer volume

The method for measurement of ulcer volume using the Kinect is demonstrated in figure 7.

The instrument is held at a distance of more than 1m away from the wound and rotated on a perpendicular plane. The sensor requires about two minutes to analyze the topography of the wound before storing the raw data for volume.

Figure: 7 Measurement of the ulcer volume using Microsoft Kinect

Analysis of scanned wound images

A preliminary algorithm for semi-automated analysis of the scanned images was implemented in Python by the Department of Bioengineering, CMC Vellore. The current analysis program works only with the depth image and does not make use of the RBG data from the wound surface, which could be used for the future enhancements of the current algorithm. The program uses the PLY file for the analysis. The first step in the analysis pipeline is the cropping of the depth image to only choose the area in and around the wound, which was carried out manually. The cropping of the 3D scan was done in Blender software by manually loading the image and using circular cropping tool. The cropped image was saved as a separate PLY file, which was used for further analysis by the IPython program. The basic algorithm used for estimating the volume of the given wound scan is given below,

1. **Generate to point cloud data:** Read the cropped PLY file and generate a point cloud data, which is a list of 3-tuples $[(x_1, y_1, z_1), (x_2, y_2, z_2) \cdots (x_n, y_n, z_n)]$, where the different x, y z in parenthesis are the individual points on the surface of the wound.
2. **Rotate point cloud data:** Depending on the orientation of the Kinect and the body during scanning, the point cloud data would have an arbitrary orientation. In order to make the analysis easier, and to have the positive

z-axis point approximately normal to the place of the body surrounding the wound, the point cloud data was rotated. The rotation angle and axis were determined by first fitting a place to the point cloud data, and finding out the angle between the normal to the plane and the positive z-axis. The axis of rotation was the axis perpendicular to the plane containing the normal to the plane and the z-axis.

3. **Contour detection:** Contour were detected on the rotated point cloud data using a built-in function in IPython, and all the closed contour detected in the point cloud data are selected and the open ones are discarded. Among the different contours, the one with the highest z-value was selected as the one that closes the wound. The xy-plane at this z value was then used for estimating the area and the volume of the wound.
4. **Area and volume estimation:** The area of the wound was calculated using the circumference data of the maximum contour selected from the previous step. The volume was calculated by using the Contour's z position and the surface of the wound falling below the contour plane.

A preliminary validation was carried out for the algorithm using handmade clay models with known volume and area. Following this, the algorithm was first applied to the different patient data.

For the three time points, this was done for both the groups as well.

The staff nurse was trained to apply a thin film (about 1mm) of Sucralfate over the pressure ulcer so as to maintain uniformity in applying the drug.

Key criteria

a. Inclusion Criteria:

1. Patients with Grade 3 pressure ulcer as per NPUAP guidelines.
2. Patients ageing 18-60 years, both sexes, any ethnicity.
3. Patients who were able to give valid consent.

b. Exclusion Criteria:

1. Wounds with necrotic tissue.
2. Patients with anaemia. (Hb< 8gm%)
3. Patients with hypoalbuminemia. (albumin< 2gm%)
4. Patient with any known renal disease was excluded.
5. H/O diabetes, connective tissue disorder, malignancy, psychiatric disorder and any other major systemic illness.

Method of randomization

In this pilot study, no randomization was done. Patients were matched according to age, sex, duration of ulcer, and PUSH 3.0 score.

Method of allocation concealment

Since this is an open-label study, allocation concealment was not required.

Blinding and masking

This was an open-label study to compare the effect of Sucralfate in comparison to normal saline in the treatment of pressure ulcers.

Primary Outcome

Reduction in PUSH scores, decrease in surface area and decrease in volume of the ulcer.

Secondary Outcome

To check for blood Aluminium levels in four (randomly chosen) patients from each group.

Target sample size and rationale

As there is no previous clinical trial of Sucralfate from which the both effect size and standard deviation can be obtained, objective sample size calculation could not be done. In one study done by Subbanna et al. in our institution, though the reduction in the healing is given in terms of mean ± SD, the SD of the control arm is too wide to be useful to be used for comparison to calculate the effect

size. There is no other literature available on the ‘rate of healing’ of pressure ulcer, therefore recruitment of matched controls was considered.

We, therefore, took 15 patients in each arm (total patients- 30) for this pilot study.

The consort flow diagram of the study is shown in the next page in figure 8.

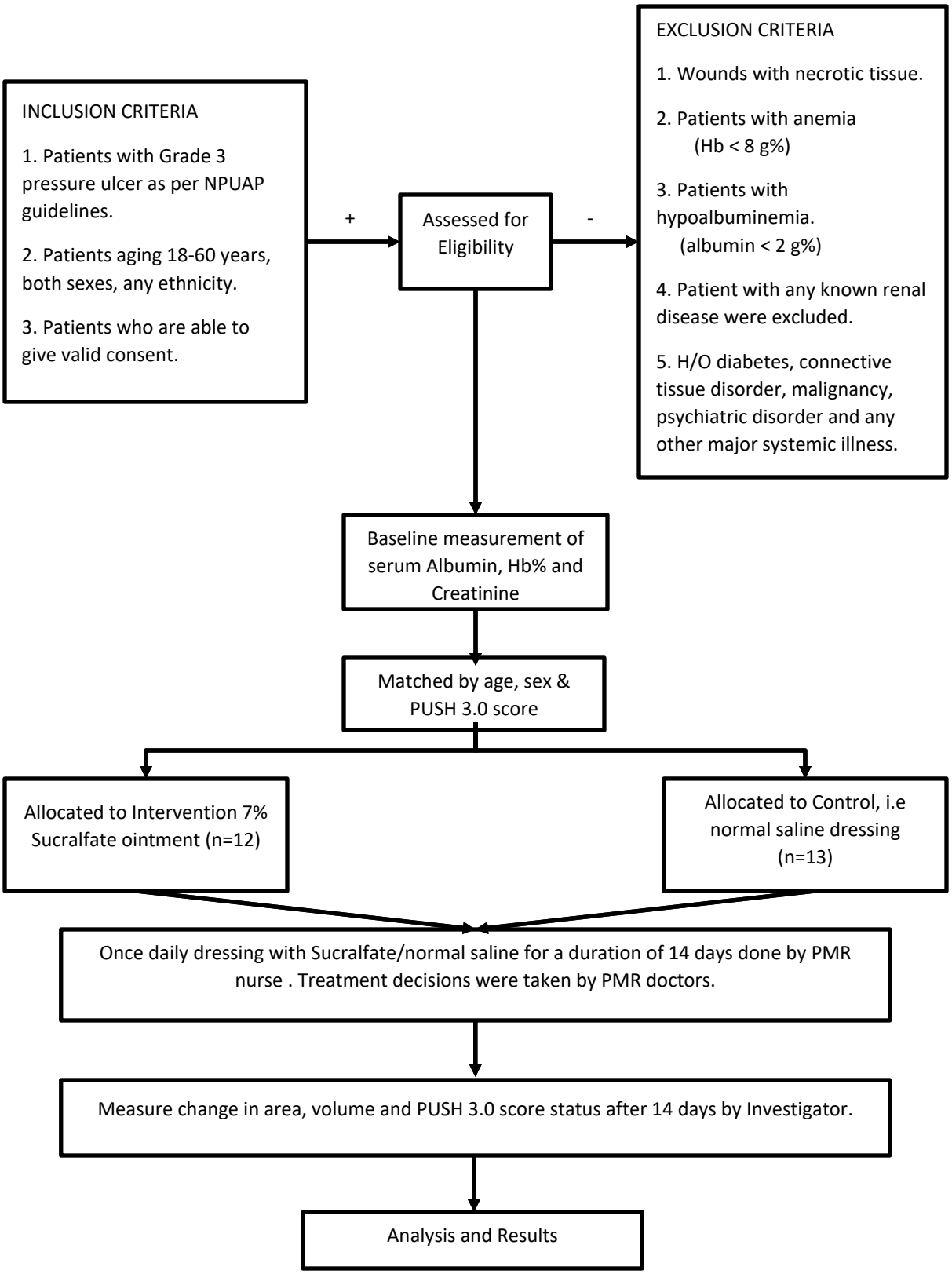

INCLUSION CRITERIA
1. Patients with Grade 3 pressure ulcer as per NPUAP guidelines.
2. Patients aging 18-60 years, both sexes, any ethnicity.
3. Patients who are able to give valid consent.
+
Assessed for Eligibility
-
EXCLUSION CRITERIA
1. Wounds with necrotic tissue.
2. Patients with anemia (Hb < 8 g%)
3. Patients with hypoalbuminemia. (albumin < 2 g%)
4. Patient with any known renal disease were excluded.
5. H/O diabetes, connective tissue disorder, malignancy, psychiatric disorder and any other major systemic illness.
Baseline measurement of serum Albumin, Hb% and Creatinine
Matched by age, sex & PUSH 3.0 score
Allocated to Intervention 7% Sucralfate ointment (n=12)
Allocated to Control, i.e normal saline dressing (n=13)
Once daily dressing with Sucralfate/normal saline for a duration of 14 days done by PMR nurse . Treatment decisions were taken by PMR doctors.
Measure change in area, volume and PUSH 3.0 score status after 14 days by Investigator.
Analysis and Results

Figure: 8 Study Flowchart

A total of 43 patients were assessed during the study period (17 months), of which 31 fulfilled the inclusion criteria and rest were excluded due to ineligibility.

Of 31 who fulfilled exclusion criteria, 6 patients refused to consent.

As a result, 25 patients were included in the study period, 13 in the normal saline group and 12 in the sucralfate group.

There were no drop-outs during the whole study period. However due to instrumental error, and once due to a patient's unavailability (went outside for investigations), we could not measure volume at a few time points.

In case of area and PUSH score 3.0, we have data in all-time points since these were measured manually.

Results

Coming to the results, both descriptive and analytical statistics were used. At the time of submission of the thesis, we have recruited 13 patients in the normal saline arm and 12 patients in the Sucralfate arm. Here we present the interim analysis for the data recorded for a total of 25 patients. The study is still ongoing with patient recruitment in progress. The baseline demographics of both groups are given in the following table.

Variables	**Saline (n=13)**	**Sucralfate(n=12)**	**p-value**
Age	30±8.33	35.83±12.15	0.1722
Sex			
Male	13(52%)	12(48%)	
Female	0(0%)	0(0%)	
Duration of Ulcer days	126.85±25.05	122.58±23.34	0.6646
Push 3.0 score	13.61±1.45	14.083±2.50	0.5687
Ulcer Volume (µl) (Median, IQR)	102.24(10.11, 344.096)	701.61(86.34,2647.16)	0.2314
Ulcer Area (sq/cm) (Median, IQR)	6.51(3.86,8.79)	14.17(6.76,27.52)	0.1419
Site			
Gluteal	0	2	
Ischial	0	2	
Sacral	10	8	
Trochanteric	3	0	
Serum Creatinine (mg/dl)	0.62±0.18	0.54±0.21	0.324
Hb (gm/dl)	12.35±1.74	11.92±2.03	0.5748
PCV (%)	35.5±4.98	34.34±5.05	0.5772
Serum albumin (gm/dl)	3.46±0.52	3.58±0.55	0.6049

Table: 1 Baseline demographic comparison between the two study groups

As we can see from the baseline demographics from table 1 after matching for age, sex and baseline PUSH 3.0 score; the baseline serum creatinine, haemoglobin, packed cell volume %, serum albumin and duration of ulcer were comparable in both the intervention group as well as the normal saline group. Respective p -values for the parameters are above 0.05, which suggest that there was no difference. The location of ulcers was mostly sacral in both groups.

Similarly, in case of initial area and volume at day 0, we also find that the p-value shows no significance. However, the median values for both these two parameters are not matched. This is most likely due to a lesser sample size and hence more variation. The volume and area data here has been presented as Median with interquartile range.

Comparison of measurements between two groups at 7th and 14th-day follow-up is given in the following table:

Variables	Saline (n=13)	Sucralfate(n=12)	p-value
Day-7			
Area(sq/cm) (Median, IQR)	4.98(2.97,8.17)	10.52(2.85,16.43)	0.446
PUSH 3.0 score	13.46±1.56	12.5±2.81	0.296
Volume (µl) (Median, IQR)	315.15(28.0,1325.05)	225.25(7.03,1441.68)	0.58
Day-14			
Area(sq/cm) (Median, IQR)	4.77(1.93,5.91)	5.48(1.87,13.70)	0.744
PUSH 3.0 score	12.08±1.71	9.08±3.8	0.017
Volume (µl) (Median, IQR)	195.45(26.24,3394.92)	41.12(0,438.64)	0.162

Table: 2 Comparison between primary outcome measurements on day 7 and 14

On day 7 and 14 median area and volume with IQR has been described in table 2. In the same table PUSH 3.0 score has been described as mean with SD.

The median volume drops in Sucralfate arm from 225.25µl to 41.12µl, whereas it drops to 195.24µl from 315.15µl in the normal saline arm. Since the p-values are 0.5795 and 0.1617 hence there is no difference in parameters between the two groups on Day 7 and 14. However, since the p-value decreases in the second week it implies that there is going towards difference.

Similarly, for the area, the median in both the groups at day 7 and day 14 do not look comparable (in spite of having a p-value more than 0.05, the IQR being on the higher side). The median area does not change much from day 7 to 14 in the normal saline arm (4.98 to 4.77), but in the Sucralfate arm, it drops to 5.48 from 10.52. Later, we found this drop to be significant.

Finally coming to the rate of healing of ulcers, it is represented in table 3

Variables	Saline (n=13)	Sucralfate(n=12)	p-value
Area 7day -Area 0day (% change)	22.879(15.394,33.088)	34.203(22.354,47.925)	0.068
Area 14day -Area 0day (% change)	35.525(29.313,55.11)	64.584(56.144,71.771)	0.002
Push 7day - Push 0day (% change)	0(0,6.6667)	12.917(10.938,17.045)	0.014
Push 14day - Push 0day (% change)	14.286(0,20)	32.292(25,41.364)	0.0002
Volume 7day - Volume 0day (% change)	30.84(-225.62,64.09)	62.617(30.75,70.927)	0.212
Volume 14day - Volume 0day (% change)	37.896(-90.626,62.751)	76.071(28.647,99.314)	0.115

Table: 3 Percentage change from baseline parameters on day 7 and day 14 between two groups (median, IQR)

Wilcoxon signed-rank test was performed to analyze the percentage change in area between the two groups from baseline. Reduction in rate of healing is explained in this table. We have the drop in the percentage of area, volume and PUSH 3.0 score from day 0 to day 7 and also for day 0 to day 14.

As evident from the table, the percentage change (decrease) in the median area on day 7 from day 0 is not significant. However, the overall percentage change(decrease) in the area on day 14 from day 0 is statistically significant.

Also, we can derive that the decrement in the percentage of the median PUSH 3.0 score on day 7 from day 0 and also on day 14 from day 0 is significant, of which the latter is more.

Coming to the volumes measured, the percentage decrease in volume in the Sucralfate arm is more compared to the normal saline arm on both days 7 and 14 from the baseline value. However, this change in percentage change of healing is not found to be statistically significant.

Adverse Events Monitoring

In a total of 25 patients across two groups, the number of adverse events is mentioned in table 4.

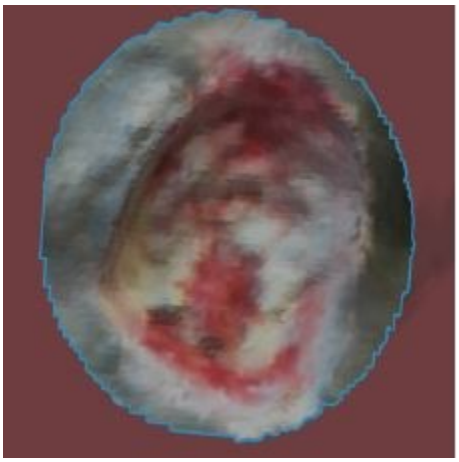
No serious adverse event occurred for these 25 patients including no death. Considering Sucralfate as a topical medicine the only case of pruritus which happened was in a 29-year-old tetraplegic subject. However, on WHO causality assessment, it was unlikely. He was managed with oral anti-histamine for three days. There was no break in the study period for the subject.

Subjects who had Urinary tract infections were managed with antibiotics as per local HICC guidelines. Rest adverse events were managed conservatively.

Adverse event	Normal saline group	Sucralfate group
Itching/Urticaria/Pruritus	0	1
Fever	1	2
Diarrhoea	3	2
Constipation	0	0
Nausea & Vomiting	2	1
Headache	0	0
Upper respiratory tract infection	1	0
Lymphadenopathy	0	0
Depression	0	0
Urinary tract infection	3	2

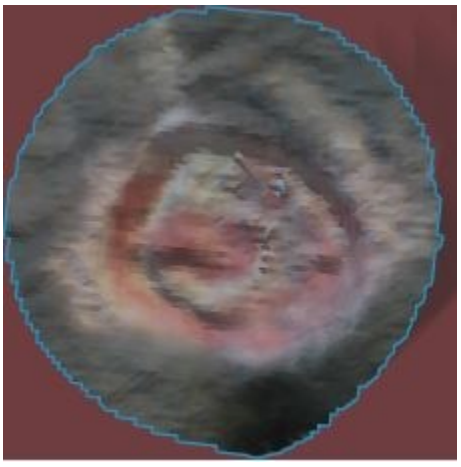
Table: 4 Number of adverse events which occurred in both the groups

Here, the cropped three-dimensional images are presented from Day 0, Day 7 and Day 14 of a T7 non-traumatic complete paraplegic patient who received the intervention(Sucralfate). The location of this particular ulcer was right ischium and it was stage 3.



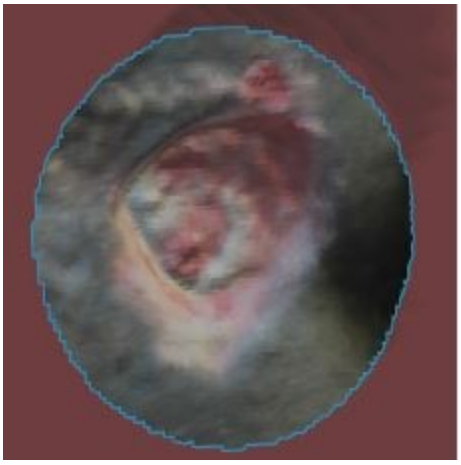
Day 0

Figure: 9a Day 0 volume recorded by Kinect of a subject(1) receiving Sucralfate



Day 7

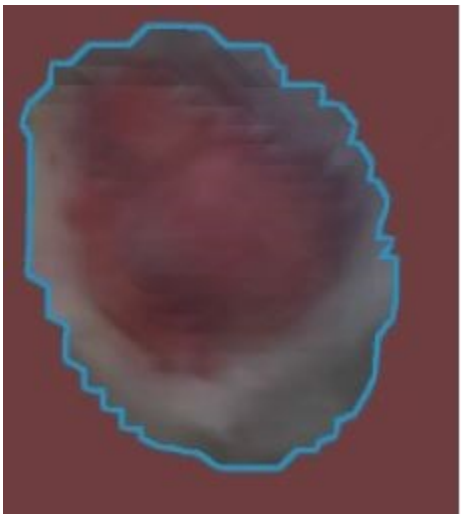
Figure: 9b Day 7 volume recorded by Kinect of a subject(1) receiving Sucralfate



Day 14

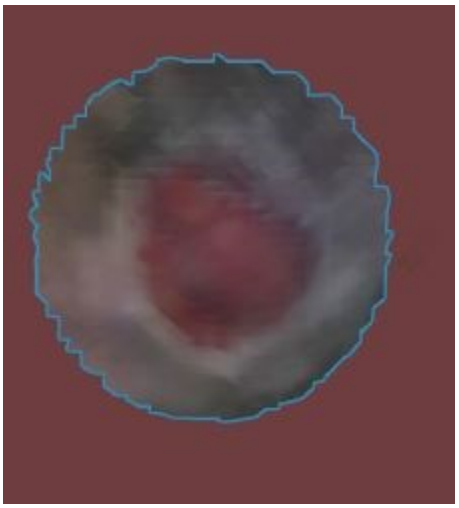
Figure: 9c Day 14 volume recorded by Kinect of a subject(1) receiving Sucralfate

Similar three-dimensional images obtained from another patient suffering from T9 paraplegia suffering from stage 3 sacral ulcer receiving Sucralfate:



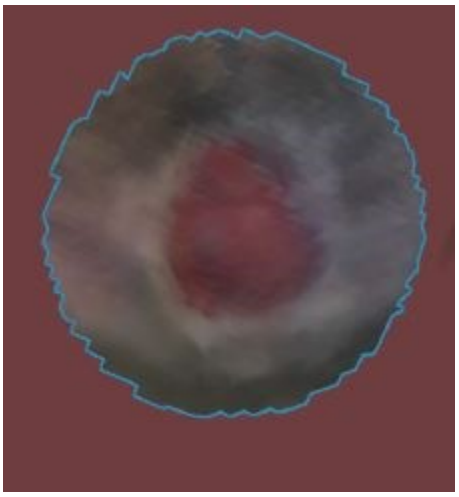
Day 0

Figure: 10a Day 0 volume recorded by Kinect of a subject(2) receiving Sucralfate



Day 7

Figure: 10b Day 7 volume recorded by Kinect of a subject(2) receiving Sucralfate



Day 14

Figure: 10c Day 14 volume recorded by Kinect of a subject(2) receiving Sucralfate

There is a visible decrement in the ulcer volume over the period over two weeks. We used the Microsoft Kinect to capture these images.

The three-dimensional mapping by which the decrease in ulcer volume was measured after getting the raw data from the Microsoft Kinect is demonstrated next. These are screenshots of volumetric data of the three-time points measured (day 0, 7 and 14) of the same patient receiving Sucralfate.

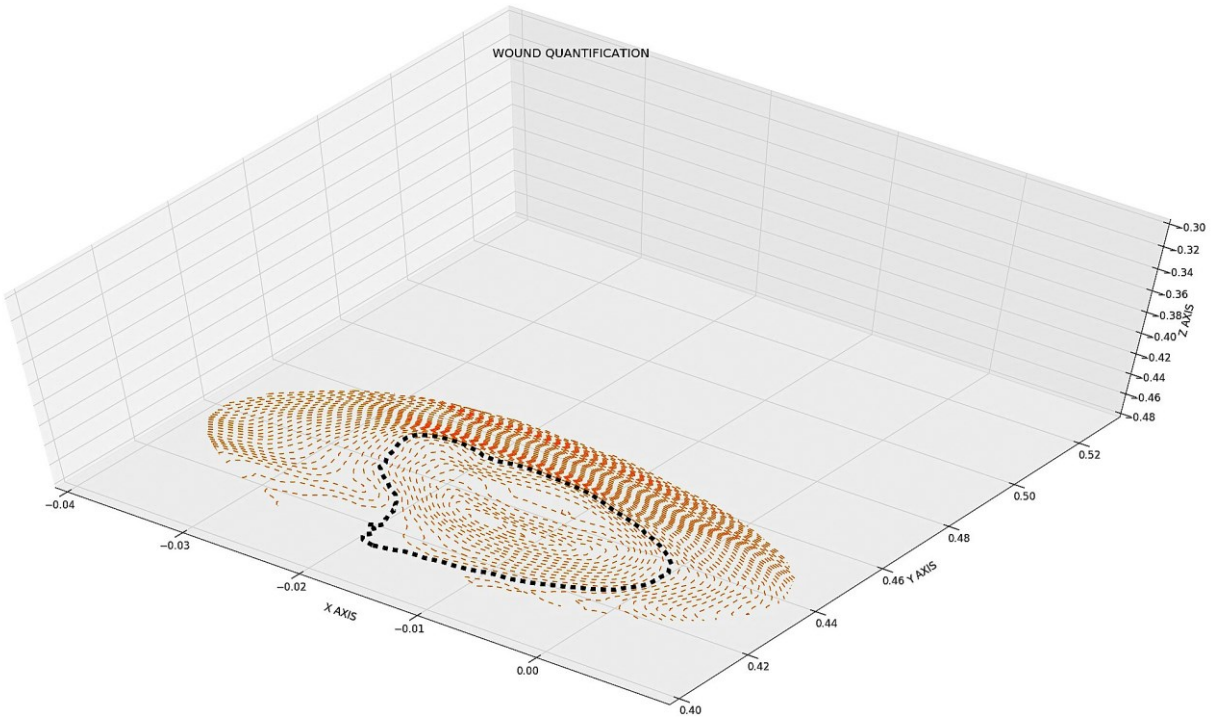


Figure: 11a Day 0 volume measurement in three-dimensional mapping of a subject

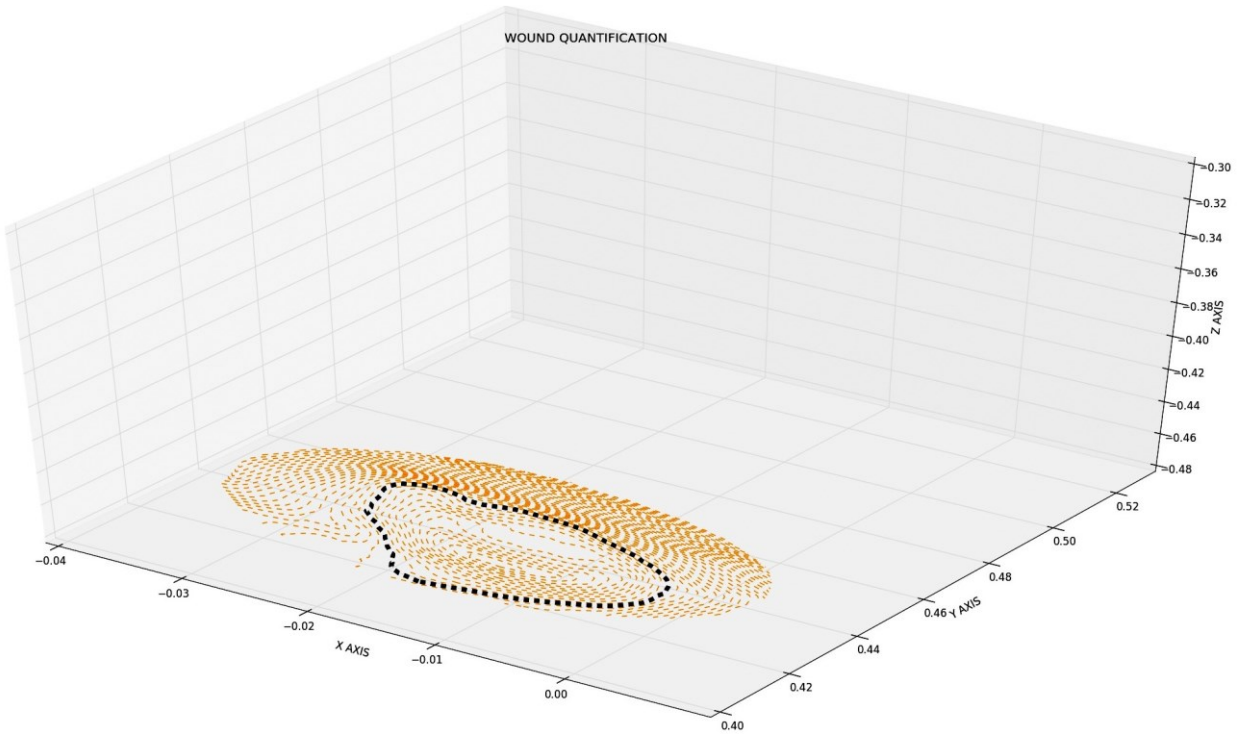


Figure: 11b Day 7 volume measurement in three-dimensional mapping of a subject

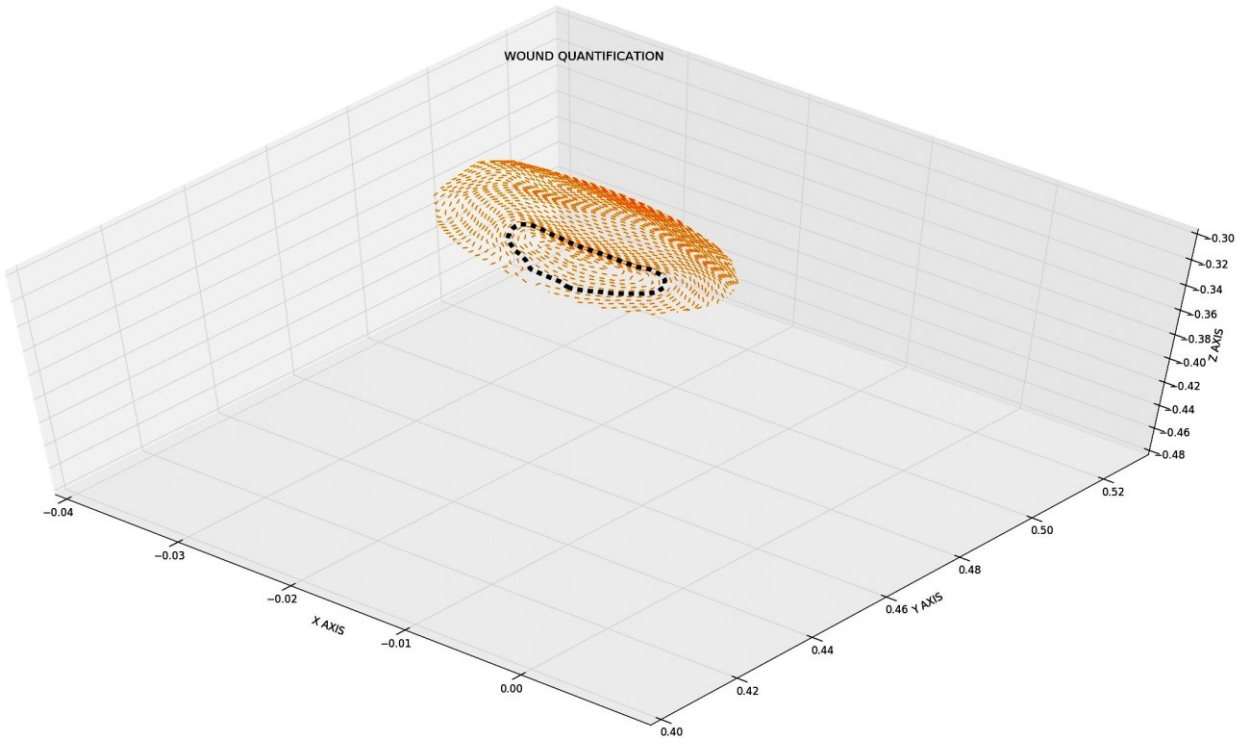


Figure: 11c Day 14 volume measurement in three-dimensional mapping of a subject

We can see over a period of two weeks the volume has decreased and it can be easily observed in figure 11.

The two-dimensional pictures of a subject who received treatment with Sucralfate, for day 0 and 7 days are shown in figure 12.

Day 0

Figure: 12a Actual picture of an ulcer on Day 0 (Sucralfate group)

Day 7

Figure: 12b Actual picture of the same ulcer(Figure 12a) on day 7 (Sucralfate group)

It is evident from the above two pictures that after a week's treatment with Sucralfate there is a visible decrease in the area along with faster healing of the wound margins.

On the contrary, the two-dimensional pictures of a subject who received treatment with normal saline dressings, for day 0 and 7 days are shown in figure 13.

Day 0

Figure: 13a Actual picture of an ulcer on Day 0 (Normal Saline group)

Day 7

Figure: 13b Actual picture of the same ulcer (Figure 13a) on day 7 (Normal Saline group)

For this patient, a week's treatment with normal saline dressings does not appear to hasten the healing process. The granulation tissue formation is less. Also, the edge of the wound is not decreasing visibly.

Discussion

Pressure ulcer poses a burden to our society even in current day settings. Management relies often on palliation and unsuccessful therapies.(88) The wound healing process is dependent on cellular proliferation, extracellular matrix remodelling, angiogenesis, tissue inflammation and good re-epithelization.(56–59) As a result, an ideal drug to manage pressure ulcers should have properties that result in improvement of all biological parameters. Dressings like alginate, hydrocolloid, hydrogel etc. are much more costly and do not have all the properties together. Sucralfate is a basic aluminium complex of sucrose sulphate which is structurally related to heparin but does not have any anticoagulant actions. Although there is a structural similarity between sucrose and Sucralfate it is not utilized as a sugar *in vivo* in humans. One of the oldest materials that were used in history for management of wounds was honey, described by Egyptians as early as 1600BC. In recent years there is an increasing interest in using sucrose as a wound dressing. Sugar, in the form of granulated sugar or pastes composed of caster and icing sugar, have been used in the management of various wounds including bedsores and diabetic ulcers.(89) Recent studies have shown the stimulating action of Sucralfate on EGF expression and also on other factors that are involved in the tissue repair process.(66) Added to this the stimulating effects of Sucralfate on the vascular factors, including angiogenesis have already been demonstrated.(67,68)

Finally, sporadic studies and case reports from the literature are all coherent indicating the favourable effect of topical sucralfate in wound and skin protection.

Surgical procedures to cover the wound like musculocutaneous flaps, skin grafts etc. are also costly procedure and increase the chances of mortality to the patient; because most of the patients have other co-morbid conditions.

Hence, there was always the need of a topical agent which can be used for the treatment of pressure ulcer which will be cheap and efficacious. Due to its ulcer healing property, Sucralfate has been used for the treatment of various types of lesions including genital, rectal, oral ulcers.(76–78) Apart from this it has been used in radiation oesophagitis as well as diaper rash.(73,80)

Having known that for the treatment of chronic ulcers theoretically, it was promising, we wanted to see the actual effect when used as a topical agent in pressure ulcers.

One group of patients were treated with topical Sucralfate and the other group received normal saline dressings, which is the standard of care, we recorded the PUSH 3.0 score, volume and area over three days (days 0, 7 and 14). The interim analysis was carried out with 25 patients' data. The trial is still ongoing.

Although the percentage change in the area did not show a significant decrease in the Sucralfate group when compared with the normal saline group till day 7, at the end of two weeks the percentage decrease in wound area was significant in the Sucralfate group, the p-value is 0.0016. Hence, it's logical to conclude that the epithelization of the wound, when treated with Sucralfate, occurs better when treated over two weeks' time. Since the area of the wound decreases better with Sucralfate, it further supports the fact that Sucralfate increases epidermal growth factor and enhances prostaglandin synthesis in keratinocytes, which is already documented in the literature.

The PUSH 3.0 score calculated from three sub-scores also showed statistically significant percentage decrease from baseline in the Sucralfate group when compared with the normal saline group both on day 7 and 14, p-values being 0.0139 and 0.0002 respectively.

The sub-scores emphasize on an approximate area, granulation tissue and exudate. Hence, it's logical to conclude Sucralfate helps in the molecular mechanism of wound healing from Day 0 itself, leading to less exudate and more granulation tissue. But, the change in area is reflected later.

When we consider the wound volume, the median of percentage decrease in the Sucralfate group is more on Day 7 and Day 14, 62.617% and 76.071% respectively, compared to decrease of 30.84% and 37.896% respectively in the

normal saline group. However, it is not statistically significant. This is most likely because of the variation in baseline volume and smaller sample size in between the two groups.

Although in our study we could not prove the change in volume to be significant, it is no doubt that this study further reinforces the molecular mechanisms mentioned elsewhere which are again reflected by the statistically significant change (decrease) in percentage area and PUSH 3.0 score in the Sucralfate group.

Conclusion

Topical Sucralfate was found to decrease the area and PUSH 3.0 score of grade 3 pressure ulcers significantly better than the standard of care normal saline commonly used in India based on our study.

This further enforces the molecular mechanisms of Sucralfate as indicated by previous studies.

However, in our study, the volume decrement in the sucralfate group is not statistically significant when compared with normal saline. The most logical reason is a smaller sample size and baseline variations in volumes between two groups.

Limitations

There were some limitations in our study like:

- The study was not blinded to subjects and investigators; only it was blinded to the person who carried out the statistical analysis. A double-blinded study gives stronger evidence.
- Due to a lesser number of patients matching the inclusion criteria, the recruitment till now is not high. This leads to the variations in baseline demographics for area and volume in between both the groups.
- We could not check for the secondary outcome of checking blood aluminium levels due to unavoidable technical failure. However, a two-month follow-up shows no change in creatinine levels from the baseline in 5 patients in the Sucralfate group.

Future scopes

This pilot study shows that the topical Sucralfate 7% ointment decreases area and PUSH 3.0 scores better than normal saline dressings. This was a phase 2 study.

The lesser sample size leads to variations in the baseline ulcer volume and area . It could not prove that the decrement in volume was significant. Hence, a larger phase 3 study done in randomized, double-blinded way needs to be done which will overcome these limitations. We would then get a better picture whether the decrease in wound volume becomes significant and it can be used as a standard treatment for the treatment of pressure ulcer.

Bibliography

1. European Pressure Ulcer Advisory Panel, National Pressure Ulcer Advisory Panel (U.S.), Pan Pacific Pressure Injury Alliance. Prevention and treatment of pressure ulcers: quick reference guide. 2014.

2. Cuddigan J, Frantz RA. Pressure ulcer research: pressure ulcer treatment. A monograph from the National Pressure Ulcer Advisory Panel. Adv Wound Care J Prev Heal. 1998 Oct;11(6):294–300; quiz 302.

3. Whitney J, Phillips L, Aslam R, Barbul A, Gottrup F, Gould L, et al. Guidelines for the treatment of pressure ulcers. Wound Repair Regen Off Publ Wound Heal Soc Eur Tissue Repair Soc. 2006 Dec;14(6):663–79.

4. Rowling JT. Pathological Changes in Mummies. Proc R Soc Med. 1961 May;54(5):409–15.

5. Pressure ulcers in America: prevalence, incidence, and implications for the future. An executive summary of the National Pressure Ulcer Advisory Panel monograph. Adv Skin Wound Care. 2001 Aug;14(4):208–15.

6. Meehan M. Multisite pressure ulcer prevalence survey. Decubitus. 1990 Nov;3(4):14–7.

7. Shahin ESM, Dassen T, Halfens RJG. Incidence, prevention and treatment of pressure ulcers in intensive care patients: a longitudinal study. Int J Nurs Stud. 2009 Apr;46(4):413–21.

8. Leblebici B, Turhan N, Adam M, Akman MN. Clinical and epidemiologic evaluation of pressure ulcers in patients at a university hospital in Turkey. J Wound Ostomy Cont Nurs Off Publ Wound Ostomy Cont Nurses Soc. 2007 Aug;34(4):407–11.

9. Reddy M, Gill SS, Kalkar SR, Wu W, Anderson PJ, Rochon PA. Treatment of pressure ulcers: a systematic review. JAMA. 2008 Dec 10;300(22):2647–62.

10. Arora M, Harvey LA, Glinsky JV, Chhabra HS, Hossain MS, Arumugam N, et al. Cost-effectiveness analysis of telephone-based support for the management of pressure ulcers in people with spinal cord injury in India and Bangladesh. Spinal Cord [Internet]. 2017 Aug 15 [cited 2017 Sep 26]; Available from: http://www.nature.com/doifinder/10.1038/sc.2017.87

11. Shojaei H, Sokhangoei Y, Soroush MR. Low Level Laser Therapy in the Treatment of Pressure Ulcers in Spinal Cord Handicapped Veterans Living in Tehran. Iran J Med Sci. 2015 Mar 29;33(1):44–8.

12. Sarabahi S, Tiwari VK, Bajaj SP. Principles and practice of wound care. New Delhi: Jaypee Brothers Medical; 2012.

13. National Pressure Ulcer Advisory Panel (NPUAP) announces a change in terminology from pressure ulcer to pressure injury and updates the stages of pressure injury | The National Pressure Ulcer Advisory Panel - NPUAP [Internet]. [cited 2017 Sep 7]. Available from: http://www.npuap.org/national-pressure-ulcer-advisory-panel-npuap-announces-a-change-in-terminology-from-pressure-ulcer-to-pressure-injury-and-updates-the-stages-of-pressure-injury/

14. Whittington KT, Briones R. National Prevalence and Incidence Study: 6-year sequential acute care data. Adv Skin Wound Care. 2004 Dec;17(9):490–4.

15. Fogerty MD, Abumrad NN, Nanney L, Arbogast PG, Poulose B, Barbul A. Risk factors for pressure ulcers in acute care hospitals. Wound Repair Regen Off Publ Wound Heal Soc Eur Tissue Repair Soc. 2008 Feb;16(1):11–8.

16. Keogh SJ, Nelson EA, Webster J, Jolly J, Ullman AJ, Chaboyer WP. Hydrocolloid dressings for treating pressure ulcers. In: Cochrane Database of Systematic Reviews [Internet]. John Wiley & Sons, Ltd; 2013 [cited 2017 Sep 26]. Available from: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010364/abstract

17. Reuler JB, Cooney TG. The pressure sore: pathophysiology and principles of management. Ann Intern Med. 1981 May;94(5):661–6.

18. Seiler WO, Stähelin HB. Skin oxygen tension as a function of imposed skin pressure: implication for decubitus ulcer formation. J Am Geriatr Soc. 1979 Jul;27(7):298–301.

19. Cifu DX, editor. Braddom's physical medicine & rehabilitation. Fifth edition. Philadelphia, PA: Elsevier; 2016. 1204 p.

20. Nussbaum EL, Biemann I, Mustard B. Comparison of ultrasound/ultraviolet-C and laser for treatment of pressure ulcers in patients with spinal cord injury. Phys Ther. 1994 Sep;74(9):812-823; discussion 824-825.

21. Management of Chronic Pressure Ulcers [Internet]. [cited 2017 Sep 26]. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3377577/

22. Bluestein D, Javaheri A. Pressure Ulcers: Prevention, Evaluation, and Management. Am Fam Physician. 2008 Nov 15;78(10):1186–94.

23. Sucralfate - DrugBank [Internet]. [cited 2017 Oct 8]. Available from: https://www.drugbank.ca/drugs/DB00364

24. Bouten CV. Literature review in behalf of the research project Etiology of pressure sores, conducted by the department of Computational and Experimental Mechanics of the Eindhoven University of Technology, in co-operation with the department of Movement Sciences of the University of [Internet]. Technical report, Department of Computational and Experimental Mechanics, Eindhoven University of Technology;

1996 [cited 2017 Sep 7]. Available from: https://www.researchgate.net/profile/Carlijn_Bouten/publication/255655594_Etiology_and_pathology_of_pressure_soresa_literature_review/links/0c960536bdd5b38764000000/Etiology-and-pathology-of-pressure-soresa-literature-review.pdf

25. Das S. A concise textbook of surgery. Calcutta: Dr S. Das; 2008.

26. Pressure ulcers prevalence, cost and risk assessment: consensus development conference statement--The National Pressure Ulcer Advisory Panel. Decubitus. 1989 May;2(2):24–8.

27. Pressure Sores: Five reviews & an RCT [Jul 1994; 6-1] [Internet]. [cited 2017 Sep 7]. Available from: http://www.bandolier.org.uk/band6/b6-1.html

28. Gerson LW. The incidence of pressure sores in active treatment hospitals. Int J Nurs Stud. 1975;12(4):201–4.

29. Shannon ML, Skorga P. Pressure ulcer prevalence in two general hospitals. Decubitus. 1989 Nov;2(4):38–43.

30. Robnett MK. The incidence of skin breakdown in a surgical intensive care unit. J Nurs Qual Assur. 1986 Nov;1(1):77–81.

31. Bergstrom N, Demuth PJ, Braden BJ. A clinical trial of the Braden Scale for Predicting Pressure Sore Risk. Nurs Clin North Am. 1987 Jun;22(2):417–28.

32. Incidence of Pressure-Sores in the Greater Glasgow Health Board Area [Internet]. PubMed Journals. [cited 2017 Sep 7]. Available from: https://ncbi.nlm.nih.gov/labs/articles/95742/

33. Kruger EA, Pires M, Ngann Y, Sterling M, Rubayi S. Comprehensive management of pressure ulcers in spinal cord injury: Current concepts and future trends. J Spinal Cord Med. 2013 Nov;36(6):572–85.

34. Fuhrer MJ, Garber SL, Rintala DH, Clearman R, Hart KA. Pressure ulcers in community-resident persons with spinal cord injury: prevalence and risk factors. Arch Phys Med Rehabil. 1993 Nov;74(11):1172–7.

35. Kosiak M. Prevention and rehabilitation of pressure ulcers. Decubitus. 1991 May;4(2):60–62, 64, 66 passim.

36. Dinsdale SM. Decubitus ulcers: role of pressure and friction in causation. Arch Phys Med Rehabil. 1974 Apr;55(4):147–52.

37. Hofman A, Geelkerken RH, Wille J, Hamming JJ, Hermans J, Breslau PJ. Pressure sores and pressure-decreasing mattresses: controlled clinical trial. Lancet Lond Engl. 1994 Mar 5;343(8897):568–71.

38. Gilchrist T, Martin AM. Wound treatment with Sorbsan--an alginate fibre dressing. Biomaterials. 1983 Oct;4(4):317–20.

39. Krapfl LA, Gray M. Does regular repositioning prevent pressure ulcers? J Wound Ostomy Cont Nurs Off Publ Wound Ostomy Cont Nurses Soc. 2008 Dec;35(6):571–7.

40. Gorse GJ, Messner RL. Improved pressure sore healing with hydrocolloid dressings. Arch Dermatol. 1987 Jun;123(6):766–71.

41. Bale S, Squires D, Varnon T, Walker A, Benbow M, Harding KG. A comparison of two dressings in pressure sore management. J Wound Care. 1997 Nov;6(10):463–6.

42. Guerrero CB. Pressure Ulcers. Quick Ref Wound Care. 2009;87.

43. Rich SE, Margolis D, Shardell M, Hawkes WG, Miller RR, Amr S, et al. Frequent manual repositioning and incidence of pressure ulcers among bedbound elderly hip fracture patients. Wound Repair Regen Off Publ Wound Heal Soc Eur Tissue Repair Soc. 2011 Jan;19(1):10–8.

44. Niezgoda JA, Mendez-Eastman S. The effective management of pressure ulcers. Adv Skin Wound Care. 2006 Feb;19 Suppl 1:3–15.

45. CARLSON B. Crawling Through the Millennia: Maggots and Leeches Come Full Circle. Biotechnol Healthc. 2006 Feb;3(1):14–7.

46. Stoddard SR, Sherman RA, Mason BE, Pelsang DJ, Sherman RM. Maggot debridement therapy. An alternative treatment for nonhealing ulcers. J Am Podiatr Med Assoc. 1995 Apr;85(4):218–21.

47. Guccione AA, Wong RA, Avers D, editors. Geriatric physical therapy. 3rd ed. St. Louis: Elsevier/Mosby; 2012. 611 p.

48. Becker H. The distally-based gluteus maximus muscle flap. Plast Reconstr Surg. 1979 May;63(5):653–6.

49. Bruck JC, Büttemeyer R, Grabosch A, Gruhl L. More arguments in favor of myocutaneous flaps for the treatment of pelvic pressure sores. Ann Plast Surg. 1991 Jan;26(1):85–8.

50. Minns RJ, Sutton RA. Carbon fibre pad insertion as a method of achieving soft tissue augmentation in order to reduce the liability to pressure sore development in the spinal injury patient. Br J Plast Surg. 1991 Dec;44(8):615–8.

51. Park S, Koh KS. Superior gluteal vessel as recipient for free flap reconstruction of lumbosacral defect. Plast Reconstr Surg. 1998 Jun;101(7):1842–9.

52. Esposito G, Ziccardi P, Di Caprio G, Scuderi N. Reconstruction of ischial pressure ulcers by skin expansion. Scand J Plast Reconstr Surg Hand Surg. 1993;27(2):133–6.

53. Healing by Intention. Adv Skin Wound Care. 2017 Jun;30(6):246–7.

54. Leaper DJ. Traumatic and surgical wounds. BMJ. 2006 Mar 4;332(7540):532–5.

55. Singer AJ, Clark RA. Cutaneous wound healing. N Engl J Med. 1999 Sep 2;341(10):738–46.

56. Eming SA, Krieg T, Davidson JM. Inflammation in wound repair: molecular and cellular mechanisms. J Invest Dermatol. 2007 Mar;127(3):514–25.

57. Werner S, Grose R. Regulation of wound healing by growth factors and cytokines. Physiol Rev. 2003 Jul;83(3):835–70.

58. Roy H, Bhardwaj S, Ylä-Herttuala S. Biology of vascular endothelial growth factors. FEBS Lett. 2006 May 22;580(12):2879–87.

59. Neal MS. Angiogenesis: is it the key to controlling the healing process? J Wound Care. 2001 Jul;10(7):281–7.

60. Hu Y, Guo S, Yan P. [Effect of local application of basic fibroblast growth factor and sucralfate on skin tissue structure after expansion]. Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi Zhongguo Xiufu Chongjian Waike Zazhi Chin J Reparative Reconstr Surg. 2002 Sep;16(5):340–4.

61. Burch RM, McMillan BA. Sucralfate induces proliferation of dermal fibroblasts and keratinocytes in culture and granulation tissue formation in full-thickness skin wounds. Agents Actions. 1991 Sep;34(1–2):229–31.

62. Tumino G, Masuelli L, Bei R, Simonelli L, Santoro A, Francipane S. Topical treatment of chronic venous ulcers with sucralfate: a placebo controlled randomized study. Int J Mol Med. 2008 Jul;22(1):17–23.

63. Candelli M, Carloni E, Armuzzi A, Cammarota G, Ojetti V, Pignataro G, et al. Role of sucralfate in gastrointestinal diseases. Panminerva Med. 2000 Mar;42(1):55–9.

64. Hollander D, Tarnawski A, Krause WJ, Gergely H. Protective effect of sucralfate against alcohol-induced gastric mucosal injury in the rat. Macroscopic, histologic, ultrastructural, and functional time sequence analysis. Gastroenterology. 1985 Jan;88(1 Pt 2):366–74.

65. Gupta PJ, Heda PS, Shrirao SA, Kalaskar SS. Topical sucralfate treatment of anal fistulotomy wounds: a randomized placebo-controlled trial. Dis Colon Rectum. 2011 Jun;54(6):699–704.

66. Konturek SJ, Konturek JW, Brzozowski T, Slomiany BL, Slomiany A. Effects of Sucralfate on Growth Factor Availability. In: Sucralfate [Internet]. Springer, Boston, MA; 1995 [cited 2017 Jul 22]. p. 175–89. Available from: https://link.springer.com/chapter/10.1007/978-0-585-32154-7_17

67. Folkman J, Szabo S, Stovroff M, McNeil P, Li W, Shing Y. Duodenal ulcer. Discovery of a new mechanism and development of angiogenic therapy that accelerates healing. Ann Surg. 1991 Oct;214(4):414-425; discussion 426-427.

68. Szabo S, Vattay P, Scarbrough E, Folkman J. Role of vascular factors, including angiogenesis, in the mechanisms of action of sucralfate. Am J Med. 1991 Aug 8;91(2A):158S–160S.

69. McCarthy DM. Sucralfate. N Engl J Med. 1991 Oct 3;325(14):1017–25.

70. Da Costa RM, Ribeiro Jesus FM, Aniceto C, Mendes M. Randomized, double-blind, placebo-controlled, dose- ranging study of granulocyte-macrophage colony stimulating factor in patients with chronic venous leg ulcers. Wound Repair Regen Off Publ Wound Heal Soc Eur Tissue Repair Soc. 1999 Feb;7(1):17–25.

71. Sweetman SC, editor. Martindale: the complete drug reference. 33. ed. London: Pharmaceutical Press; 2002. 2483 p.

72. Mantoo S, Raina VK. Topical sucralfate : role in the prevention and healing of skin excoriations around enterostomas, Gastro-intestinal fistulas and perineal region. J Indian Assoc Pediatr Surg. 1997 Feb 1;2(4):126.

73. Markham T, Kennedy F, Collins P. Topical sucralfate for erosive irritant diaper dermatitis. Arch Dermatol. 2000 Oct;136(10):1199–200.

74. Burkhart CG, Black C, Burkhart CN. A Topical Application Containing Sucralfate, Zinc Oxide and Ketoconazole Provides High Patient Satisfaction in the Treatment of Intertrigo. Open Dermatol J. 2009 Feb 10;3(1):11–3.

75. Lentz SS, Barrett RJ, Homesley HD. Topical sucralfate in the treatment of vaginal ulceration. Obstet Gynecol. 1993 May;81(5 (Pt 2)):869–71.

76. Alpsoy E, Er H, Durusoy C, Yilmaz E. The use of sucralfate suspension in the treatment of oral and genital ulceration of Behçet disease: a randomized, placebo-controlled, double-blind study. Arch Dermatol. 1999 May;135(5):529–32.

77. Lin P, Liang G. Behçet disease: recommendation for clinical management of mucocutaneous lesions. J Clin Rheumatol Pract Rep Rheum Musculoskelet Dis. 2006 Dec;12(6):282–6.

78. Gupta PJ, Heda PS, Kalaskar S, Tamaskar VP. Topical sucralfate decreases pain after hemorrhoidectomy and improves healing: a randomized, blinded, controlled study. Dis Colon Rectum. 2008 Feb;51(2):231–4.

79. Etiz D, Erkal HS, Serin M, Küçük B, Hepari A, Elhan AH, et al. Clinical and histopathological evaluation of sucralfate in prevention of oral mucositis induced by radiation therapy in patients with head and neck malignancies. Oral Oncol. 2000 Jan;36(1):116–20.

80. Sur RK, Kochhar R, Singh DP. Oral sucralfate in acute radiation oesophagitis. Acta Oncol Stockh Swed. 1994;33(1):61–3.

81. Banati A, Chowdhury SR, Mazumder S. Topical use of Sucralfate Cream in second and third degree burns. Burns J Int Soc Burn Inj. 2001 Aug;27(5):465–9.

82. Tryba M, Mantey-Stiers F. Antibacterial activity of sucralfate in human gastric juice. Am J Med. 1987 Sep 28;83(3B):125–7.

83. Volkin DB, Verticelli AM, Marfia KE, Burke CJ, Mach H, Middaugh CR. Sucralfate and soluble sucrose octasulfate bind and stabilize acidic fibroblast growth factor. Biochim Biophys Acta. 1993 Nov 10;1203(1):18–26.

84. Temir ZG, Karkiner A, Karaca I, Ortaç R, Ozdamar A. The effectiveness of sucralfate against stricture formation in experimental corrosive esophageal burns. Surg Today. 2005;35(8):617–22.

85. Masuelli L, Tumino G, Turriziani M, Modesti A, Bei R. Topical use of sucralfate in epithelial wound healing: clinical evidences and molecular mechanisms of action. Recent Pat Inflamm Allergy Drug Discov. 2010 Jan;4(1):25–36.

86. Thomas DR, Rodeheaver GT, Bartolucci AA, Franz RA, Sussman C, Ferrell BA, et al. Pressure ulcer scale for healing: derivation and validation of the PUSH tool. The PUSH Task Force. Adv Wound Care J Prev Heal. 1997 Sep;10(5):96–101.

87. PUSH Tool 3.0 (web version) | The National Pressure Ulcer Advisory Panel - NPUAP [Internet]. [cited 2017 Oct 4]. Available from: http://www.npuap.org/resources/educational-and-clinical-resources/push-tool/push-tool/

88. Mekkes JR, Loots M a. M, Van Der Wal AC, Bos JD. Causes, investigation and treatment of leg ulceration. Br J Dermatol. 2003 Mar;148(3):388–401.

89. Thomas S. Wound management and dressings. London: Pharmaceutical Press; 1990. 211 p.

Annexures

Institutional Review Board approval letter:

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Ethics Committee Registration No: ECR/326/INST/TN/2013 issued under Rule 122D of the Drugs & Cosmetics Rules 1945, Govt. of India

Dr. George Thomas, D Ortho Ph.D.
Chairperson, Ethics Committee

Dr. B. Antonisamy, M.Sc., Ph.D., FSMS, FRSS.
Secretary, Research Committee

Prof. Keith Gomez, B.Sc., MA (S.W), M.Phil.
Deputy Chairperson, Ethics Committee

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho.
Chairperson, Research Committee & Principal

Dr. Nihal Thomas,
MD, MNAMS, DNB (Endo), FRACP (Endo), FRCP (Edin), FRCP (Glasg)
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

October 16, 2015

Dr. Jayanta Kumar Dey
PG Registrar
Department of Pharmacology and Clinical Pharmacology,
Christian Medical College,
Vellore

Sub: **Fluid Research grant project NEW PROPOSAL:**
A prospective, open label, pilot study to evaluate the role of Sucralfate in the management of pressure ulcers.
Dr. Jayanta Kumar Dey (Emp. No. 21211), Pharmacology and Clinical Pharmacology, Dr. Margaret Shanthi FX (Emp. No. 50156), Pharmacology and Clinical Pharmacology, Dr. A. Blessed Winston (Emp. No. 28839), Pharmacology, Mr. Aniket Kumar (Emp. No. 32592), Pharmacology, Dr. Prashanth H. Chalageri (Emp. No. 20777), PMR, Dr. Henry Prakash (Emp. No. 20322), PMR, Dr. Swapna Patil, (Emp. No. 20322), PMR, Dr. Shiva Balasubramaniam (Emp. No. 33767), Bioengineering, Dr. S. Annadurai (Emp. No. 30526), Pharmacy.

Ref: IRB Min. No. 9533(INTERVEN) dated 22.07.2015

Dear Dr. Jayanta Kumar Dey,

I enclose the following documents:-

1. Institutional Review Board approval 2. Agreement

Could you please sign the agreement and send it to Dr. Nihal Thomas, Addl. Vice Principal (Research), so that the grant money can be released.

With best wishes,

Dr. NIHAL THOMAS
MD.,MNAMS.,DNB(Endo),FRACP(Endo),FRCP(Edin),FRCP(Glasg)
SECRETARY (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

Dr. Nihal Thomas
Secretary (Ethics Committee)
Institutional Review Board

1 of 6

Ethics Committee Silver, Office of Research, I Floor, Carman Block, Christian Medical College, Vellore, Tamil Nadu 632 002
Tel: 0416 – 2284294, 2284202 Fax: 0416 – 2262788 E-mail: research@cmcvellore.ac.in

OFFICE OF RESEARCH
INSTITUTIONAL REVIEW BOARD (IRB)
CHRISTIAN MEDICAL COLLEGE, VELLORE, INDIA

Ethics Committee Registration No: ECR/326/INST/TN/2013 issued under Rule 122D of the Drugs & Cosmetics Rules 1945, Govt. of In

October 16, 2015

Dr. Jayanta Kumar Dey
PG Registrar
Department of Pharmacology and Clinical Pharmacology,
Christian Medical College,
Vellore

Sub: **Fluid Research grant project NEW PROPOSAL:**
A prospective, open label, pilot study to evaluate the role of Sucralfate in the manageme pressure ulcers.
Dr. Jayanta Kumar Dey (Emp. No. 21211), Pharmacology and Clinical Pharmacology, Dr. Margaret Shanthi FX (Emp. No. 50156), Pharmacology and Clinical Pharmacology, Dr. A. Blessed Winston (Emp. No. 28839), Pharmacology, Mr. Aniket Kumar (Emp. No. 32592), Pharmacology, Dr. Prashanth H. Chalageri (Emp. No. 20777), PMR, Dr. Henry Prakash (Emp. No. 20322), PMR, Dr. Swapna Patil, (Emp. No. 20322), PMR, Dr. Shiva Balasubramaniam (Emp. No. 33767), Bioengineering, Dr. S. Annadurai (Emp. No. 30526), Pharmacy.

Ref: IRB Min. No. 9533(INTERVEN) dated 22.07.2015

Dear Dr. Jayanta Kumar Dey,

The Institutional Review Board (Silver, Research and Ethics Committee) of the Christian Medical College, Vellore, reviewed and discussed your project titled "A prospective, open label, pilot study to evaluate the role of Sucralfate in the management of pressure ulcers" on July 22nd 2015.

The Committee reviewed the following documents:

1. IRB Application format
2. Informed Consent Form and Patient Information Sheet (English, Tamil, Hindi, Bengali)
3. Proforma
4. Cvs of Drs. Jayanta Kumar Dey, Margaret Shanthi FX, Blessed Winston, Prashanth H. Chalageri , Swapna Patil, Shiva Balasubramaniam , Aniket Kumar.
5. No. of documents 1 – 5

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Chairperson, Ethics Committee

Dr. B. Antonisamy, M.Sc., Ph.D., FSMS, FRSS.
Secretary, Research Committee

Prof. Keith Gomez, B.Sc., MA (S.W), M.Phil.
Deputy Chairperson, Ethics Committee

Dr. Alfred Job Daniel, D Ortho MS Ortho DNB Ortho.
Chairperson, Research Committee & Principal

Dr. Nihal Thomas,
MD, MNAMS, DNB (Endo), FRACP (Endo), FRCP (Edin), FRCP (Glasg)
Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

The following Institutional Review Board (Silver, Research & Ethics Committee) members were present at the meeting held on July 22nd2015 at 9.45 am in the CREST/SACN Conference Room, Christian Medical College, Bagayam, Vellore 632002.

Name	Qualification	Designation	Affiliation
Dr. B. Antonisamy	MSc, PhD, FSMS, FRSS	Professor, Biostatistics, Secretary (Research Committee), IRB, CMC, Vellore	Internal, Statistician
Dr. Nihal Thomas	MD, MNAMS, DNB(Endo), FRACP (Endo) FRCP(Edin) FRCP (Glasg)	Professor & Head, Endocrinology, Additional Vice Principal (Research), Deputy Chairperson (Research Committee), Member Secretary (Ethics Committee), IRB, CMC, Vellore	Internal, Clinician
Dr. D. J. Christopher	BSc, MBBS, DTCD DNB, FRCP(Glasg), FCCP(USA)	Professor, Pulmonary Medicine, Associate Director (HR), CMC, Vellore	Internal, Clinician
Dr. Anuradha Bose	MBBS, DCH, MD,MRCP, FRCPCH	Professor, Child Health, CMC, Vellore	Internal, Clinician
Dr. B. Poonkuzhali	MSC, PhD	Professor, Haematology, CMC, Vellore	Internal, Basic Medical Scientist
Dr. Suresh Devasahayam	BE, MS, PhD	Professor of Bio-Engineering, CMC, Vellore	Internal, Basic Medical Scientist

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Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Dr. Biju George	MBBS, MD, DM	Professor, Haematology, CMC, Vellore	Internal, Clinician
Dr. Molly Jacob	MBBS, MD, PhD	Professor, Biochemistry, CMC, Vellore	Internal, Clinician
Dr. George Thomas	MBBS, D Ortho, PhD	Orthopaedic Surgeon, St. Isabella Hospital, Chennai, Chairperson, Ethics Committee, IRB.	External, Clinician
Prof. Keith Gomez	BSc, MA (S.W), M. Phil (Psychiatry Social Work)	Student counselor, Loyola College, Chennai, Deputy Chairperson, Ethics Committee, IRB	External, Lay Person & Social Scientist
Mr. Samuel Abraham	MA, PGDBA, PGDPM, M. Phil, BL.	Sr. Legal Officer, CMC, Vellore	Internal, Legal Expert
Dr. P. Zachariah	MBBS, PhD	Retired Professor, Vellore	External, Clinician
Mrs. Pattabiraman	BSc, DSSA	Social Worker, Vellore	External, Lay person
Dr. Jayaprakash Muliyil	BSC, MBBS, MD, MPH, Dr PH (Epid), DMHC	Retired Professor, CMC, Vellore	External, Scientist & Epidemiologist
Dr. Shirley David	MSc, PhD	Professor, Head of Fundamentals Nursing Department, College of Nursing, CMC, Vellore	Internal, Nurse
Mr. C. Sampath	BSc, BL	Advocate, Vellore	External, Legal Expert
Rev. Dr. T. Arul Dhas	MSc, BD, DPC, PhD(Edin)	Chaplaincy Department, CMC, Vellore	Internal, Social Scientist

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Deputy Chairperson,
Secretary, Ethics Committee, IRB
Additional Vice-Principal (Research)

Dr. Binu Susan Mathew	MBBS, MD	Associate Professor, Clinical Pharmacology CMC, Vellore	Internal, Pharmacologist
Mrs. Ruma Nayak	M Sc (Nursing)	Professor, Head of Paediatric Nursing & Deputy Nursing Superintendent, College of Nursing, CMC, Vellore	Internal, Nurse

We approve the project to be conducted as presented.

The Institutional Ethics Committee expects to be informed about the progress of the project, any **adverse events** occurring in the course of the project, any **amendments in the protocol and the patient information / informed consent**. On completion of the study you are expected to submit a copy of the **final report**. Respective forms can be downloaded from the following link: http://172.16.11.136/Research/IRB_Polices.html in the CMC Intranet and in the CMC website link address: http://www.cmch-vellore.edu/static/research/Index.html.

The study will need to be submitted to a three monthly **Data Safety Monitoring Board** (DSMB) review with duly filled in form found in the link
http://172.16.11.136/Research/IRB_Polices.html

The trial need to be registered with **Clinical Trial Registry India** (CTRI) http://ctri.nic.in before commencing.

Kindly provide the total number of patients enrolled in your study and the total number of withdrawals for the study entitled: "A prospective, open label, pilot study to evaluate the role of Sucralfate in the management of pressure ulcers "on a monthly basis. Please send copies of this to the Research Office (research@cmcvellore.ac.in)

IRB Min. No. 9533(INTERVEN) dated 22.07.2015 5 of 6

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Fluid Grant Allocation:
A sum of 75,000/- INR (Rupees Seventy five Thousand only) will be granted for 18 months and out of which a maximum of Rs 5,000/- can be spent for stationery, printing, Xeroxing and computer charges (if computers used are within the institution).

Yours sincerely,

Dr. Nihal Thomas
Secretary (Research Committee)
Institutional Review Board

Dr. NIHAL THOMAS
MD, MNAMS, DNB(Endo), FRACP(Endo), FRCP(Edin), FRCP(Glasg)
SECRETARY - (ETHICS COMMITTEE)
Institutional Review Board,
Christian Medical College, Vellore - 632 002.

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Participant information sheet and informed consent form:

PATIENT INFORMATION SHEET

Title of the Study: A Prospective Open-label Pilot study, evaluating the role of Sucralfate in comparison to normal saline for the management of Pressure Ulcers

Introduction

I am Dr. Jayanta Kumar Dey from the Dept. of Pharmacology doing a study on a newer treatment modality in bedsores and will give you information to be a part of the study. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of the study doctor, the staff or me.

Purpose of the research

Currently normal saline dressings are used as treatment apart from surgery (which is costly) for bedsores. The reason why we are doing this study is to see whether Sucralfate works better than normal saline in healing of bedsores.

Type of Research Intervention & Duration

This study will involve your bed sore being dressed with a 7% ointment of Sucralfate once daily for 14 days.

Participant selection

We are inviting all patients admitted with bedsores in the age group of 18-60 years irrespective of ethnicity and sex in the Department of PMR, CMC Vellore.

Voluntary Participation

Your participation in this research is entirely voluntary. Your decision to participate or not, will not in anyway affect the services you will get in this institution. You can change your mind through the study and can withdraw even if you agreed earlier.

Your Responsibility

To provide, to the best of your knowledge, complete information about your current medical condition and past medical history, including current illness, prior hospitalizations, current medications, allergies, and all other health-related matters(including those during this study).

Information on the Trial Drug [Sucralfate]

The drug we are testing in this study is called Sucralfate. It is an approved drug for peptic ulcer disease and other skin ailments. We now want to test this drug topically on bedsores.

Procedures and Protocol

To test whether the new drug works better, we will put people taking part in this study into two groups selected by matching of ulcer area. Participants in one group will be given the test drug while participants in the other group will be given the normal saline dressings. You will know which group you are into. We will be checking blood Aluminium levels free of cost for four random patients in each group.

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Side Effects and Risks

To the best of the available knowledge no side effect is anticipated. There is a faint risk that your bedsore will not get better and that Sucralfate doesn't work even as well as the old one, in which case, we will provide you with the standard treatment.

Benefits

There may not be any benefit for you but your participation is likely to help us find the answer to the research question. There may not be any benefit to the society at this stage of the study, but future generations are likely to benefit, if the study succeeds.

Confidentiality

The information that we collect from this research project will be kept confidential. Information about you that will be collected during the research will be put away and no one but the researchers will be able to see it. However we may use the data obtained for further studies without compromising your identity. It will not be shared with or given to anyone unless it is legally required.

Right to Refuse or Withdraw

This is a reconfirmation section. You do not have to take part in this research if you do not wish to do so. You may also stop participating in the research at any time you choose. It is your choice and all of your rights will still be respected.

Alternatives to Participating

If you do not wish to take part in the research, you will be provided with the established standard treatment available at the hospital. People who have bed sores are given normal saline dressings and you will receive the same.

Contact person for any queries

If you have any questions you may contact any of the following:

- Dr. Jayanta Kumar Dey

Department of Pharmacology, CMC, Vellore.
Phone No: 0416 2284237
Email: drjayanta86@cmcvellore.ac.in

- Dr. Prashanth H. Chalageri

Department of Physical Medicine and Rehabilitation, CMC, Vellore.
Phone No: 0416 2285274
Email: drpachi@gmail.com

Investigator's Name: Jayanta Kumar Dey

Investigator's Signature: _____ Date: ____/____/_____

Informed Consent form to participate in a research study:

Study Title: Use of sucralfate as a healing agent in bed sores in comparison to normal saline.

Study Number: _____

Hospital Id: _____

Subject's Initials: _____ **Subject's Name:** _____

Date of Birth / Age: _____

(Subject)

(i) I confirm that I have read and understood the information sheet dated _____ for the above study and have had the opportunity to ask questions. [ ]

(ii) I understand that my participation in the study is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. [ ]

(iii) I understand that the Ethics Committee and the regulatory authorities will not need my permission to look at my health records both in respect of the current study and any further research that may be conducted in relation to it, even if I withdraw from the trial. I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published. [ ]

(iv) I agree not to restrict the use of any data or results that arise from this study provided such a use is only for scientific purpose(s). [ ]

(v) I agree to take part in the above study. [ ]

Signature (or Thumb impression) of the Subject/Legally Acceptable

Date: ____/____/_____

Signatory's Name: _____ Signature:

Or

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Representative: _____

Date: ____/____/_____

Signatory's Name: _____

Signature of the Investigator: _____

Date: ____/____/_____

Study Investigator's Name: _____

Signature or thumb impression of the Witness: _____

Date: ____/____/_____

Name & Address of the Witness: _____

Data collection form:

Proforma for Data Collection: Sucralfate on Pressure Ulcer Trial

Name: Date:

Hospital Number: Drug Allocation Number:

Date of Birth / Age:

Sex:

Primary Diagnosis:

Location of Pressure ulcer:

Day	Actual Area(cm^2)	PUSH 3.0 score				Volume of the ulcer(cm^3)	Remarks
		Area	Exudate amount	Tissue type	Total		
0		Length X Width	none/light/moderate/heavy	closed/epithelial/granulation/slough/necrotic			
7							
14							